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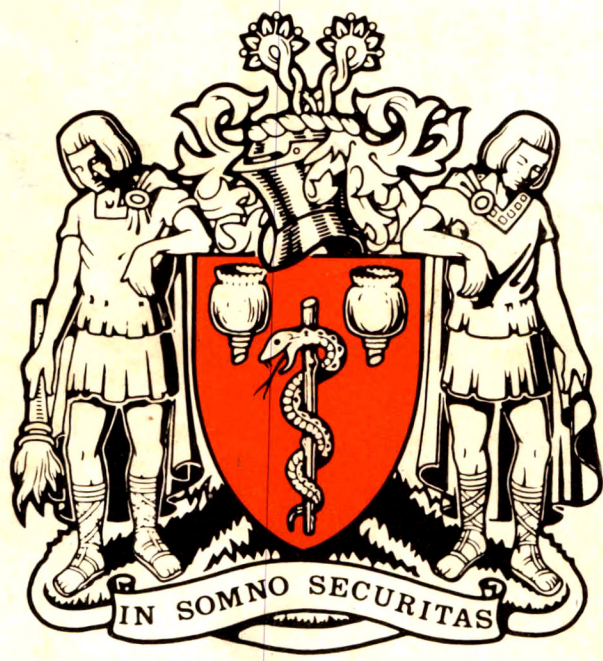
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Anaesthesia

Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 43 Number 1 January 1988

6



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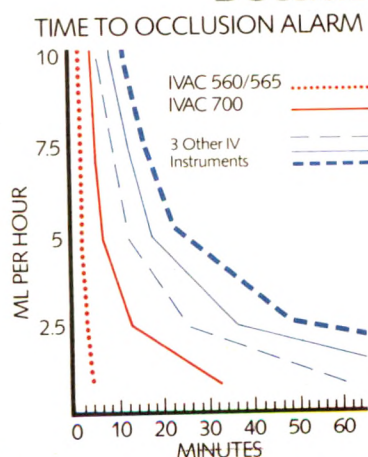
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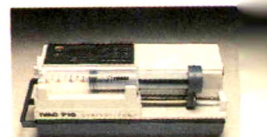
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Anaesthesia

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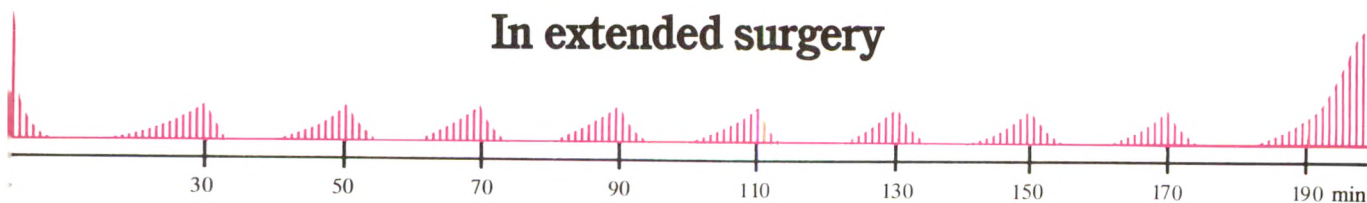
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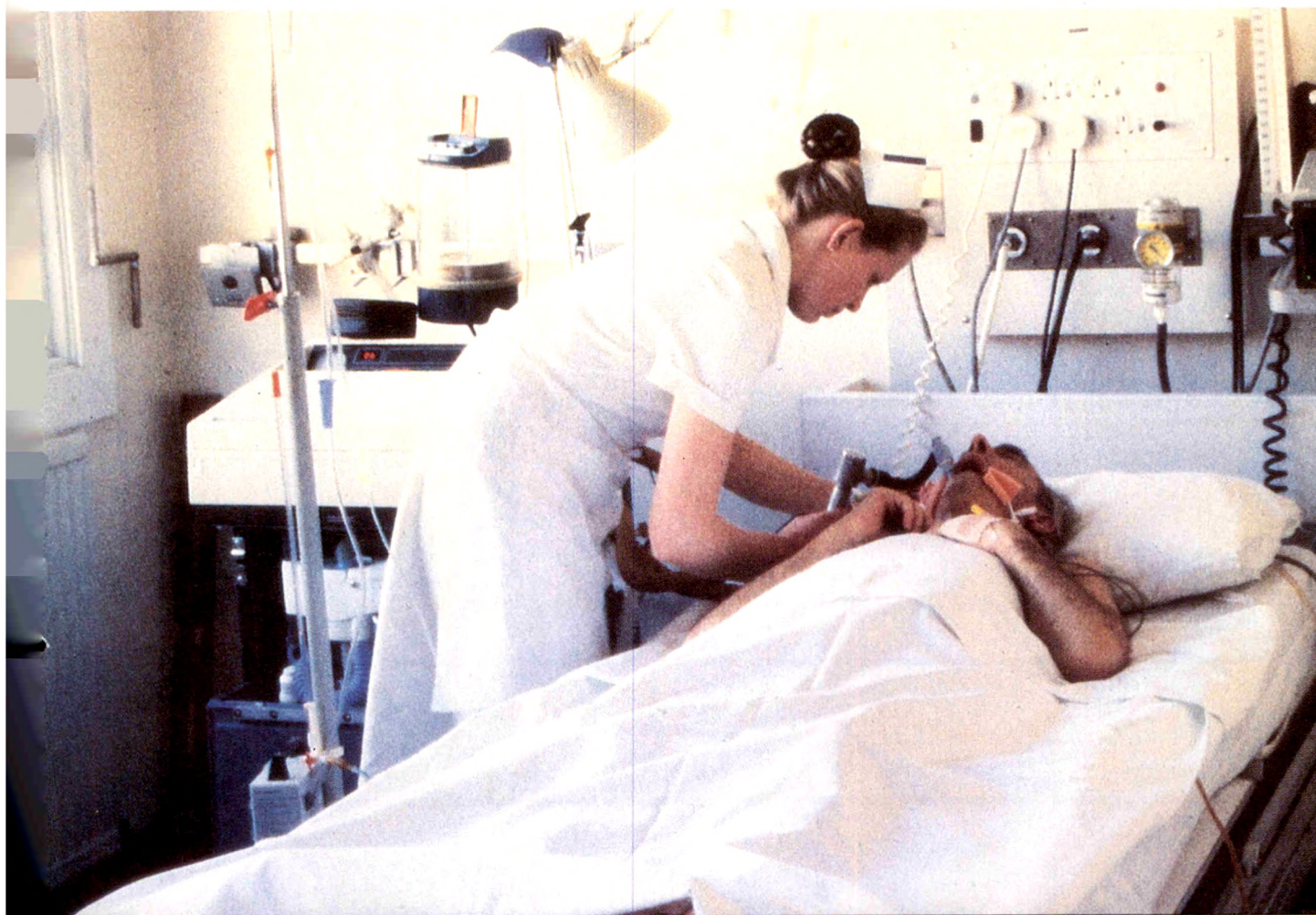
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1. Data on file, Wellcome, 1987.
2. Yate, P.M. *et al.* (1986), *Br. J. Anaesth.*, **58**, 112 S.

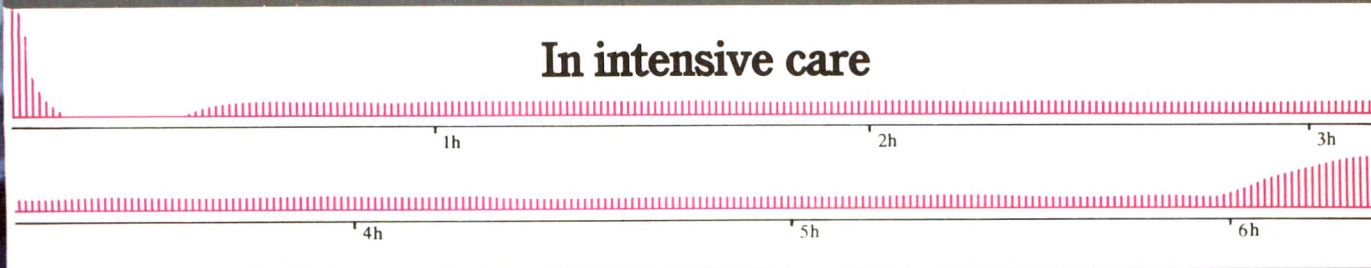
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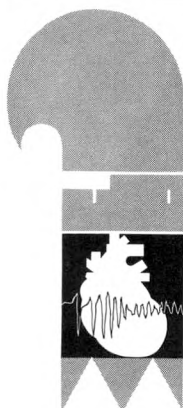
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Ohmeda Technical Report

Insurance against signal interference: detection and minimization in pulse oximetry.

Pulse oximeters rely on plethysmographic pulsations to determine oxygen saturation levels.¹ There is no doubt that signal interference in pulse oximetry monitoring can cause erroneous SaO₂ readings. This interference has been well documented.^{2,3,4} Because of the inescapable phenomenon of signal interference, two capabilities are required in pulse oximetry technology.

The first requirement: continuously displayed plethysmographic waveform.

Pulse oximeters that display an arterial plethysmographic waveform have an advantage over those that display only the pulse amplitude of the signal. The waveform allows the operator to assess the quality of the signal from which the arterial oxygen saturation is derived, and to observe noise, which may alter its accuracy.⁵

The value of a waveform is that you can tell if you are getting a real physiological signal.⁶ With a displayed arterial waveform or plethysmograph, interference is easily detected by the shape of the waveform. On a non-waveform oximeter, a bouncing pulse indicator does not give the clinician any information on the integrity of the shape of the arterial waveform. Interference from a fiberoptic light source, surgical lighting, or infrared heat lamps might go undetected, and erroneous SaO₂ readings might be accepted as valid.^{7,8,9}

The second requirement: selective signal processing. Quantity, weighting, and averaging.

Pulse oximeters that make multiple readings during the cardiac cycle, rather than a single calculation at the peak and trough, have more data to compensate for artifactual changes.¹⁰

The Ohmeda pulse oximeter performs thirty SaO₂ calculations every second, rather than one per beat, so that enough data are provided for intelligent, selective processing. The objective is to gather enough data to permit some discrimination during selective processing, while maintaining a rapid response time. Selective processing is then done by "weighting" each SaO₂ calculation and "averaging" the weighted data.

Weighting.

With this large number of data points, it is possible to selectively "weight" each one. The Ohmeda pulse oximeter uses many criteria to qualify the validity of each data point and determine the appropriate weight. These include the magnitude of change in the amplitude of the waveform, the point in the cardiac cycle, the "newness" of the data, and the correlation to the present "average" saturation.

Example: When interference is present, the "noise" spikes typically have extreme amplitude changes. Consequently, the weighting of these unnaturally large amplitudes is lower, thereby minimizing the effect of interference.

Example: Interference can cause the instantaneous SaO₂ value to be significantly different than the current "average" saturation, so these outlying SaO₂ values are weighted lower. The greater the difference, the lower the weighting.

For instance, if the present "average" saturation is 96% and the next data point is calculated to be 72% (due to interference compromising the calculation), this data point will be given a low weight. If an instantaneous value of 50% is calculated, it will be given an even lower weight. Intuitively, we know this dramatic change in the patient's saturation could not occur in 1/30th of a second.

The weighting factor allows a discounting of physiologically implausible differences in each instantaneous SaO₂ value, thereby reducing the effect of interference on displayed SaO₂ readings—without the additional confusion of ECG leads, extra cables, and heavy interconnect boxes.

Averaging.

The individually weighted data points are then averaged over a selectable 3, 6, or 12 second interval. In a six-second period, the oximeter has 180 data points from which to calculate SaO₂. If a very fast response or optimum resolution in SaO₂ changes is necessary, the faster three-second response mode is available. During periods of prolonged interference, the capability to extend the averaging time allows for the collection and weighting of enough data to derive a valid, stable saturation reading.

In monitoring SaO₂, it is necessary to have reliable readings for patient safety. Signal interference can be detected and minimized with optimal data collection, signal processing, and continuous waveform display.

¹Unprecedented Rise in Use of Pulse Oximetry Reflects Important Advance in Anesthesiology. **Anesthesiology News**, July 1987, pp 1, 66, 68–69. ²Block FE Jr: Interference in a Pulse Oximeter from a Fiberoptic Light Source. **Journal of Clinical Monitoring**, July 1987, pp 210–211. ³Pulse Oximeter Interference from Surgical Lighting. **Health Devices**, February 1987, pp 50–51. ⁴Brooks T, Paulus D, Winkle W: Infrared Heat Lamps Interfere with Pulse Oximeters. **Anesthesiology**, November 1984, p 630. ⁵Taylor MB, Norley I: Correspondence "Erroneous Actuation of the Pulse Oximeter." **Anaesthesia**, 42:10:116, October 1987. ⁶Gravenstein NS: Technical Note. **Oximetry Update**, Edition 3, Summer 1986. ⁷Same as footnote 2. ⁸Same as footnote 3. ⁹Same as footnote 4. ¹⁰Same as footnote 1.

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Editorial

The evolution of *Anaesthesia*

This Editorial is intended to record some of the changes which have occurred recently and which are of sufficient, albeit perhaps limited interest, to all our readers. The first and the most obvious is that the page size of this number of the journal is increased. The change was partly the result of the inevitable march of time; indeed, many of our contemporaries in the world have already made this improvement. Some of our friends will, no doubt, be sorry to see the small-sized journal disappear, and the need to adapt shelves may annoy others, but the shelf length occupied by future numbers of *Anaesthesia* will not immediately match that of the past. There were few alternatives to this decision, which was made by the Editorial Board, and we hope it will be approved by our readers.

1987 saw the introduction of *Anaesthesia News*. The experiment is, thus far, a success and from this issue we intend to publish monthly. *Anaesthesia News* is circulated to all members of the Association of Anaesthetists of Great Britain and Ireland and is their opportunity to communicate promptly with their colleagues everywhere. One of our main reasons for its introduction was to increase the space in the journal for articles. The immediate effect was modest but now, coupled with the increase in page size, we may be able significantly to decrease the delay between acceptance of an article and its appearance in print.

Gradually over the last five years, *Anaesthesia* has changed its policy about peer review. This is an important matter, debated vigorously by editors of medical and scientific journals throughout the world and there is no general agreement about the validity, necessary extent or even desirability of external review! Suffice to say here that our review of manuscripts often extends beyond the five Editors and is usually double-blind, that is to say, that neither the reviewer is told the identity of the authors, nor the author(s) that of the reviewers. We believe that this process may help us in our quest for quality.

No development can happen in an organisation like a journal without the considerable contribution of many people. The Assistant Editors play a substantial part in the process of peer review but the Editorial Board of *Anaesthesia* do not, except as individual experts, have this role. Nevertheless, amongst the members of the Board were two Advisory Editors: Drs R.S. Atkinson and T.B. Boulton. Dr Atkinson resigned early in 1987 after many years' service to the journal, first as an Assistant Editor and then, since 1980, as an Advisory Editor. Dr Boulton, previously Assistant Editor and Editor, was forced, by pressure of other duties, also to relinquish his post recently. No-one can ever know the extent of the contribution these men made to our journal. Fortunately, for the writer, they have both agreed to continue to counsel him when required but meanwhile, we all thank both of them sincerely for all their unstinting service.

The acceptance of a manuscript by one of the Editors signals the start of a laborious and painstaking process. The Assistant Editors supervise this and, with the assistance of our publishers (currently and happily serviced by Mr Ray Aller), produce final copy for printing. That production process includes our librarians' check of the references and the Editors' attention to all the matters of house style which go to make up the final appearance of our journal. This team of Assistants deserves considerable praise, not only for their work but also for the donation of their time. No editor has a better team and it is right that their contribution should be publicly acknowledged.

Finally, we have sadly to announce that Dr Philip J. Helliwell, John Snow Silver Medallist and Past President, has decided to retire from his Chairmanship of the Editorial Board. He has been our Chairman since 1976 and has guided with a gentle but effective touch the deliberations of the Board; all its members, and the members of the Association, want to thank him again and to wish him well.

J. N. LUNN

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (*British Medical Journal* 1979; 1: 532-5). Details will be found in the Notice of Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Halothane and isoflurane in outpatient anaesthesia

A comparison of recovery

K. R. MILLIGAN, J. P. HOWE AND J. W. DUNDEE

Summary

The speed and quality of recovery after anaesthesia were studied in 60 outpatients. Anaesthesia was induced using propofol and maintained by nitrous oxide in oxygen supplemented with either halothane or isoflurane. Initial clinical recovery was significantly faster in the halothane group but no differences were found during subsequent psychomotor testing. Minor postoperative side effects were common in both groups.

Key words

Anaesthesia; outpatient.

Anaesthetics, volatile; halothane, isoflurane.

Isoflurane is a halogenated ether which has a lower blood/gas solubility coefficient than halothane; this should result in a more rapid recovery than that associated with the older inhalational agents.¹ This is of special relevance to outpatient anaesthesia, where rapid and uneventful recovery is of prime importance. However, the case for isoflurane in outpatient practice has yet to be established; it is expensive, and studies in children have shown that isoflurane produces a higher incidence of unsatisfactory induction than halothane, with no benefits in terms of recovery.^{2,3} McAteer *et al.*⁴ confirmed a higher incidence of side effects at induction and found recovery to be inferior to that following halothane. Carter *et al.*⁵ were unable to show any difference in recovery after either halothane or isoflurane anaesthesia in adults when methohexitone was used for induction. They suggested the hypothesis that any difference between the inhalational agents was small in relation to the effect of methohexitone.

The purpose of the present study was to compare the speed and quality of recovery in two groups of patients in whom anaesthesia was induced with propofol and maintained with equipotent concentrations of either halothane or isoflurane. Propofol was chosen as the induction agent because immediate recovery is rapid and, in the absence of inhalational agents, its effect on postoperative psychomotor testing disappears quickly.⁶ The study was confined to patients in whom anaesthesia had lasted for a minimum of 15 minutes, both to reduce the effect of the induction agent and because there is evidence that these patients are more prone to postoperative complications.^{7,8}

Methods

Sixty fit, unpremedicated patients who underwent outpatient operations were included in the study; these were 30 males (vasectomy) and 30 females (minor gynaecological procedures). Half of the male and female patients were allocated randomly to receive halothane (group H) and the other half received isoflurane (group I). Patients were aged between 18 and 55 years and weighed 45-85 kg; none was receiving concomitant medication. Informed consent was obtained from each patient and the protocol was approved by the University Medical Research Ethical Committee.

Anaesthesia was induced with propofol 2.5 mg/kg injected over 20 seconds and maintained, via a Bain system, with 67% nitrous oxide in oxygen supplemented by either halothane or isoflurane. The volatile agents were administered via a Cyprane Fluotec 3 or a Cyprane Fortec vaporizer, the calibration of which had been checked using an Engstrom Emma multigas analyser. The concentration of the volatile agent was increased in three increments over the first minute of induction to either 2.5% isoflurane or 1.5% halothane; these doses are equipotent.¹ These concentrations were maintained until the end of the surgical procedure. The duration of anaesthesia was recorded as the time from the start of induction until the end of surgery. A note was made of any adverse side effects.

Recovery was assessed by a second anaesthetist who was unaware of the volatile agent used. Initial clinical recovery was assessed by recording the times from the end of surgery until the unstimulated patients could open their eyes on

K.R. Milligan, MB, FFARCS, Research Fellow, J.P. Howe, MD, FFARCS, Consultant, J.W. Dundee, MD, PhD, FRCP, FFARCS, Professor, Department of Anaesthetics, The Queen's University and Mater Infirmorum Hospital, Belfast.

Accepted 3 June 1987.

command, give their correct date of birth and demonstrate orientation in time and place.

Subsequent clinical recovery (the patient's alertness and coordination) was assessed subjectively at 30, 60 and 90 minutes after operation. Alertness was assessed using a four-point scale (4, fully awake; 3, drowsy but awake; 2, sleeping but rousable; 1, unrousable) and coordination by straight-line walking and Romberg's test.

Psychomotor testing was carried out using a four-choice reaction time (CRT)⁹ and Treiger tests.¹⁰ The time allowed for CRT testing was 150 seconds; these assessments were carried out twice pre-operatively to familiarise the patients with the apparatus and the Treiger test. The results of the first series were discarded and the results of the second taken as pre-operative baseline values. Subsequent testing was carried out 30, 60 and 90 minutes postoperatively. The incidence of any minor postoperative sequelae such as headache and nausea was also noted.

The results were analysed using the Mann-Whitney *U* test, Chi squared and Fisher's exact probability test as appropriate.

Results

The 30 patients in each group were comparable in respect of age, weight and duration of anaesthesia (Table 1). There was no significant difference between groups in the number of patients who experienced side effects at induction; coughing or laryngospasm occurred in two patients in group H and four in group I. Anaesthesia and operation conditions were satisfactory in all cases. Initial recovery after anaesthesia was significantly faster in group H than in group I for all three endpoints (Table 2).

Subsequent clinical recovery was similar in both groups. Seventeen group H and 18 group I patients demonstrated

ataxia 30 minutes postoperatively but no patient was affected at 60 minutes. Thirty minutes postoperatively in group I were considered to be drowsy (grade 3) compared to 16 in group H. One group H but no group I patient considered to be grade 2. All patients except one in group I were considered to be fully alert (grade 4) 60 minutes after operation.

Table 3 summarises the choice reaction times in two groups. There were no differences between the groups at any time as assessed by either CRT or by the Treiger tests.

Postoperative headache was commoner in group I than in group H (13) but the difference was not statistically significant. Postoperative emesis was rare; one group H patient vomited and one group I patient complained of nausea. All patients were considered to be fit for discharge by the completion of testing. Only one patient (group I) was unwilling to receive the same anaesthetic on any occasion; a severe postoperative headache was cited as the reason.

Discussion

The pharmacological profile of isoflurane (low blood partition coefficient, low biodegradation) suggests that it provides at least some of the characteristics of an agent suitable for use in outpatients. Despite this, the results of our study and those of others⁴⁻⁵ show that although satisfactory in terms of recovery from anaesthesia, it has no advantages over halothane. Our finding of a quicker initial recovery in the halothane group is in agreement with that of McAteer *et al.*⁴ but this is unlikely to be of great significance in the clinical situation, since the differences between the groups had disappeared by 30 minutes. It should be noted, however, that equipotent inhaled concentrations do not necessarily result in equipotent alveolar concentrations, since a variety of factors (e.g. respiratory minute volume, cardiac output, blood solubility) affect the difference between inspired and alveolar concentration. Alveolar equipotency could be achieved and monitored if it is possible that a difference might be found between the two agents in terms of recovery.

In this study we anaesthetised outpatients with equivalent inspired concentrations of halothane and isoflurane. Both agents provided satisfactory anaesthesia and recovery.

Table 1. Mean (SD) values for patient age, weight and duration of anaesthesia.

	Halothane group (H)	Isoflurane group (I)
Age, years	34.7 (7.0)	34.2 (7.0)
Weight, kg	68.5 (9.3)	64.6 (9.2)
Duration, minutes	20.5 (2.6)	21.0 (2.4)

Table 2. Mean, median and quartiles for initial clinical recovery times. Differences between groups were significant ($p < 0.05$) for all endpoints.

Time (minutes)	Halothane group (H)			Isoflurane group (I)		
	Mean	Median	Quartiles	Mean	Median	Quartiles
Eye opening	9.1	9.3	7.4-11.3	11.1	10.4	9.0-13.0
Giving date of birth	9.6	9.4	7.6-11.8	11.6	10.9	9.8-13.3
Orientation	9.9	10.0	7.9-11.8	11.9	11.3	10.1-13.5

Table 3. Mean, median and quartiles for pre- and postoperative choice reaction times.

Choice reaction time (milliseconds)	Halothane group (H)			Isoflurane group (I)		
	Mean	Median	Quartiles	Mean	Median	Quartiles
Pre-operative	506	489	419-580	499	449	411-541
30 minute postoperative	598	561	499-642	592	545	470-652
60 minute postoperative	494	473	413-544	504	461	410-536
90 minute postoperative	461	436	391-528	465	441	397-494

but isoflurane was found to offer no advantages over halothane in terms of recovery from anaesthesia.

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References

1. EGER EI. Isoflurane: a review. *Anesthesiology* 1981; **55**: 559-76.
2. PANDIT UA, STEUDE GM, LEACH AB. Induction and recovery characteristics of isoflurane and halothane anaesthesia for short outpatient operations in children. *Anaesthesia* 1985; **40**: 1226-30.
3. CATTERMORE RW, VERGHESE C, BLAIR IJ, JONES CJH, FLYNN PJ, SEBEL PS. Isoflurane and halothane for outpatient dental anaesthesia in children. *British Journal of Anaesthesia* 1986; **58**: 385-9.
4. MCATEER PM, CARTER JA, COOPER GM, PRYS-ROBERTS C. Comparison of isoflurane and halothane in outpatient paediatric dental anaesthesia. *British Journal of Anaesthesia* 1986; **58**: 390-3.
5. CARTER JA, DYE AM, COOPER GM. Recovery from day-case anaesthesia. The effect of different inhalational anaesthetic agents. *Anaesthesia* 1985; **40**: 545-8.
6. MILLIGAN KR, O'TOOLE DP, HOWE JP, COOPER JC, DUNDEE JW. A comparison of incremental propofol with propofol-isoflurane for outpatient gynaecological surgery. *British Journal of Anaesthesia* 1987; **59**: (in press).
7. OGG TW. An assessment of postoperative outpatient cases. *British Medical Journal* 1972; **4**: 573-6.
8. FAHY A, MARSHALL M. Postanaesthetic morbidity in outpatients. *British Journal of Anaesthesia* 1969; **41**: 433-8.
9. WILKINSON RT, HOUGHTON D. Portable four-choice reaction time test with magnetic tape memory. *Behavioural Research Methods and Instrumentation* 1975; **7**: 441-6.
10. NEWMAN MG, TREIGER N, MILLER JC. Measuring recovery from anaesthesia—a simple test. *Anesthesia and Analgesia* 1969; **48**: 136-40.

Isoflurane as an alternative to halothane for Caesarean section

R. G. GHALY, R. J. FLYNN AND J. MOORE

Summary

Two series of 25 patients who underwent elective Caesarean section with general anaesthesia were given either 0.75% isoflurane or 0.5% halothane as supplements to 50% nitrous oxide in oxygen used for maintenance. The potent inhalational agent was given for the entire operative period and no case of intra-operative dreaming or awareness was reported. The infusion dose of suxamethonium was significantly less with isoflurane, 50 µg/kg/minute (SD 17), as compared to halothane, 64 µg/kg/minute (SD 24) ($p < 0.02$). Recovery from anaesthesia was more rapid with isoflurane. The surgeon's assessment of uterine relaxation and bleeding using a visual analogue score indicated that this was significantly less with isoflurane. Infant well-being as judged by Apgar score and cord blood gas analysis, showed little difference between the two inhalational agents.

Key words

Anaesthesia; obstetric.

Anaesthetics, inhalational; halothane, isoflurane.

The use of nitrous oxide-oxygen alone for the maintenance of general anaesthesia in obstetrics is associated with an unacceptable incidence of awareness.¹ The addition of a low concentration of halothane has been shown to reduce the incidence of this complication without any increase in other maternal or fetal complications.² Isoflurane has gained wide acceptance and in many situations replaces halothane but it has not been investigated extensively for obstetric use. This study in women who underwent elective Caesarean section compared the maternal and fetal effects of supplementation of 50% nitrous oxide in oxygen with either 0.5% halothane or 0.75% isoflurane.

Methods

Patients selected for the study were healthy, had an uncomplicated pregnancy of greater than 37 weeks' gestation and were to be delivered by elective Caesarean section for cephalopelvic disproportion. They were randomly allocated to either the isoflurane or halothane group. All gave informed verbal consent for inclusion in the investigation, which had the approval of the local ethical committee.

After an intravenous infusion of compound sodium lactate solution was established, and with lateral tilt and pre-oxygenation, anaesthesia was induced with thiopentone 3-5 mg/kg followed by suxamethonium 100 mg to facilitate rapid tracheal intubation. Maintenance of anaesthesia was with 50% nitrous oxide in oxygen supplemented by either

0.5% halothane or 0.75% isoflurane, which were continued until the beginning of skin closure. Alfentanil 1.0 mg was given intravenously following delivery and the nitrous oxide concentration was increased to 70%. Neuromuscular block was maintained by infusion of suxamethonium 0.1% at a rate of administration just sufficient to abolish diaphragmatic movement. The total amount of suxamethonium used was determined gravimetrically. Ventilation was adjusted to maintain an end tidal carbon dioxide of 4-4.25 kPa using a Datex Normocap. The concentration of the inhalational supplement was checked continuously by an Engström Emma. Oxytocin 5 units was given intravenously at delivery to promote uterine contraction, and a further increment of similar amount was given if requested by the surgeon for continued uterine relaxation or if there was bleeding.

The mother's ECG was monitored continuously and her arterial blood pressure checked automatically by Dinamap recorder before and at 5-minute intervals throughout the operative period. Maternal arterial and umbilical venous and arterial blood, the latter from a double-clamped portion of umbilical cord, were collected at delivery for immediate estimation of pH, P_{O_2} and P_{CO_2} values using a Corning 178 pH blood gas analyser. The Apgar scores of infants were determined at 1 and 5 minutes by a neonatologist who was unaware of the inhalational agent used.

The surgeon graded uterine relaxation on an unmarked 10-cm visual analogue scale; the zero point indicated none and the 10 mark severe relaxation, respectively. This, to-

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gether with the need for supplementary doses of oxytocin, gave a clinical indication of the degree of uterine relaxation. The mother's pre- and postoperative (at 24 hours) haemoglobin and haematocrit were recorded. All mothers were questioned during the first postoperative day about intra-operative dreaming or awareness.

Statistical analysis was performed using the unpaired Student's *t*-test; *p* < 0.05 was considered to be significant.

Results

Fifty patients divided equally between the halothane and isoflurane groups, were studied. The two series were closely comparable with regard to age, weight and duration of anaesthesia (Table 1).

The induction dose of thiopentone, the amount of suxamethonium infused together with the induction-delivery and uterine incision-delivery times, are given in Table 2. None of the differences shown is statistically significant but the dose of suxamethonium given on a µg/kg/minute basis was significantly less in the isoflurane group, 50 µg/kg/minute (SD 17), as compared to 64 µg/kg/minute (SD 24) in the halothane group (*p* < 0.02).

Cardiovascular changes during the induction-delivery

interval are affected markedly by tracheal intubation in a lightly anaesthetised patient.³ Here 19 and 15 patients, respectively, in the isoflurane and halothane groups had increases in both systolic and diastolic arterial blood pressure greater than 5 mmHg. Hypotension during this time, defined as a systolic reading below 100 mmHg, occurred in three and two patients given isoflurane and halothane, respectively.

Data related to uterine relaxation and bleeding are shown in Table 3. The surgeon's assessments of relaxation indicated that this was significantly less with isoflurane (*p* < 0.03) and only four patients in this series required additional oxytocin as compared to eight given halothane. The pre- and postoperative haemoglobin and haematocrit values concur with the anaesthetist's assessment that no patient required blood transfusion for intra-operative loss.

The Apgar scores, together with the maternal arterial and umbilical venous and arterial blood pH, *PO*₂ and *PCO*₂ estimations, are shown in Table 4. The 1-minute Apgar scores are significantly higher for infants of mothers who received isoflurane (*p* = 0.02, Mann-Whitney *U* test), but none of the other differences is significant.

The time from cessation of anaesthesia, during which the mothers breathed 100% oxygen, until rejection of the tracheal tube was significantly shorter for isoflurane (2.6 minutes, SD 1.4) as compared to halothane (4.4 minutes, SD 2.0) (*p* < 0.001). None of the mothers complained of intra-operative dreams or awareness.

Discussion

The addition of a potent inhalational agent to nitrous oxide-oxygen has the advantage of allowing the use of a

Table 1. Mean (SD) age, weight and duration of anaesthesia for the isoflurane and halothane series.

Treatment	Age, years	Weight, kg	Duration of anaesthesia, minutes
Isoflurane (<i>n</i> = 25)	28 (6)	78 (13)	47 (13.4)
Halothane (<i>n</i> = 25)	28 (4)	77 (18)	46 (13.2)

Table 2. Mean (SD) induction dose of thiopentone, total amount of suxamethonium infused and relevant operation times for the isoflurane and halothane series.

Treatment	Dosage		Time, minutes	
	Thiopentone, mg/kg	Suxamethonium, mg	Induction-delivery	Uterine incision-delivery
Isoflurane (<i>n</i> = 25)	3.83 (0.77)	174 (63)	10.4 (3.0)	2.2 (1.4)
Halothane (<i>n</i> = 25)	3.74 (0.87)	204 (73)	11.0 (3.8)	1.9 (0.9)

Table 3. Pre- and postoperative haemoglobin and haematocrit values, together with visual analogue score (VAS) assessment of uterine relaxation and need for additional oxytocin treatment for the isoflurane and halothane groups. Values expressed as mean (SD).

Treatment	Haemoglobin, g/dl		Haematocrit		VAS assessment of uterine relaxation	Additional doses of Syntocinon
	Pre-operative	Postoperative	Pre-operative	Postoperative		
Isoflurane (<i>n</i> = 25)	11.8 (0.8)	11.4 (0.7)	0.35 (0.02)	0.34 (0.03)	3.8 (1.8)	4
Halothane (<i>n</i> = 25)	12.1 (1.1)	11.6 (1.2)	0.36 (0.03)	0.35 (0.03)	4.8 (1.6)	8

Table 4. Mean Apgar scores (range) at 1 and 5 minutes together with mean (SD) maternal arterial and umbilical venous and arterial pH, *PO*₂ and *PCO*₂ at delivery.

Treatment	Apgar scores		Maternal arterial			Umbilical arterial			Umbilical venous		
	1 minute	5 minutes	pH	<i>PO</i> ₂ , kPa	<i>PCO</i> ₂ , kPa	pH	<i>PO</i> ₂ , kPa	<i>PCO</i> ₂ , kPa	pH	<i>PO</i> ₂ , kPa	<i>PCO</i> ₂ , kPa
Isoflurane (<i>n</i> = 25)	7.4 (5-8)	8.9 (7-9)	7.36 (0.05)	19.1 (8.9)	4.2 (1.0)	7.26 (0.05)	3.5 (1.0)	6.1 (1.0)	7.30 (0.05)	4.6 (1.4)	5.6 (1.2)
Halothane (<i>n</i> = 25)	6.7 (4-8)	8.8 (8-10)	7.37 (0.05)	21.9 (5.7)	4.4 (0.8)	7.27 (0.04)	3.2 (0.7)	6.6 (1.1)	7.30 (0.03)	4.9 (0.8)	5.9 (0.8)

higher inspired oxygen concentration⁴ and, possibly, the benefit to the placental circulation of an increased uterine blood flow,⁵ as well as a decreased incidence of intra-operative awareness. In high concentrations these agents cause uterine relaxation⁶ and, since they are highly lipid soluble, un-ionised and of low molecular weight, their rapid placental transfer would increase the incidence of infant depression. Halothane 0.5% has proved to be satisfactory² since it eliminates maternal awareness, promotes uterine blood flow and does not affect infant well-being. Nevertheless, previous exposure to this agent, especially in the recent past, introduces a risk of hepatotoxicity.⁷ Therefore, a comparison of isoflurane with halothane seemed appropriate.

The addition of 0.75% isoflurane to the inspired mixture of 50% nitrous oxide in oxygen was not associated with intra-operative dreaming or awareness in this investigation. The depressant effects of halothane and isoflurane on the circulation differ⁸ but their use here did not show significant variation during the induction-delivery period. Hypotension with either agent was easily corrected by increasing uterine displacement to relieve caval occlusion.

Both the phase 1 and phase 2 neuromuscular blocks produced by suxamethonium are prolonged by isoflurane.^{9,10} In the present study a significant reduction in the amount of suxamethonium infused was recorded in the patients given this agent. It should also be noted that isoflurane enhances the action of nondepolarising relaxants to a greater extent than does halothane,¹¹ which indicates a need for careful dosage in the obstetric patient.

Isoflurane did not increase uterine relaxation or bleeding when used in 0.75% concentration throughout the operation. Such use has the advantage of further decreasing the likelihood of maternal awareness. It is difficult to assess blood loss accurately during Caesarean section but the method used here seemed to give a reliable estimation. No patient required blood transfusion and the pre- and post-operative haemoglobin and haematocrit changes did not indicate excessive blood loss. However, it should be remembered that isoflurane, like other inhalational agents, causes a dose-related depression of uterine contractility⁶ and higher concentrations will increase bleeding.

The condition of the infant at birth as determined by Apgar score was better at 1 minute with isoflurane, but no difference between the series was recorded at 5 minutes. The blood pH and gas studies did not suggest any impairment of placental perfusion or fetal circulation with either agent. The fetal effects of similar concentrations of isoflurane and halothane in patients who underwent delivery by Caesarean section were investigated by Warren *et al.*¹² and they reported that lactate levels in umbilical arterial blood were comparable. They concluded that infant meta-

bolic acidosis due to placental insufficiency did not with either agent.

This investigation has shown that 0.75% isoflurane can be used instead of 0.5% halothane for maintenance of general anaesthesia in the obstetric patient. Its use throughout the entire period of anaesthesia is advocated as this further decrease the likelihood of maternal awareness. Isoflurane significantly reduced the amount of suxamethonium required for muscle relaxation. Neither uterine relaxation nor bleeding presented difficulty and infant well-being was not affected. Recovery from anaesthesia was more rapid than with halothane.

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References

1. WILSON J, TURNER DJ. Awareness during Caesarean section under general anaesthesia. *British Medical Journal* 1980; **280**: 3.
2. MOIR DD. Anaesthesia for Caesarean section. An evaluation of a method using low concentrations of halothane and 100% oxygen. *British Journal of Anaesthesia* 1970; **4**: 42.
3. LOUGHRAN PG, MOORE J, DUNDEE JW. Maternal response associated with caesarean delivery under general anaesthesia. *British Journal of Obstetrics and Gynaecology* 1986; **93**: 943-9.
4. MARX GF, MATEO CV. Effects of different oxygen concentrations during general anaesthesia for elective Caesarean section. *Canadian Anaesthetists' Society Journal* 1971; **18**: 587-9.
5. PALAHNIUK RJ, SHNIDER SM. Maternal and fetal cardiovascular and acid-base changes during halothane anaesthesia in the pregnant ewe. *Anesthesiology* 1971; **41**: 462-72.
6. MUNSON ES, EMBRO WJ. Enflurane, isoflurane, and halothane and isolated human uterine muscle. *Anesthesiology* 1971; **53**: 11-14.
7. BLOGG CE. Halothane and the liver: the problem revisited. *British Medical Journal* 1986; **292**: 1691.
8. JONES RM. Clinical comparison of inhalation anaesthetics. *British Journal of Anaesthesia* 1984; **56**: 57S-69S.
9. MILLER RD, WAY WL, DONAL WM, STEVENS WC, EMMETT J. Comparative neuromuscular effects of pancuronium bromide, succinylcholine, and succinylcholine during Forane and halothane anaesthesia in man. *Anesthesiology* 1971; **35**: 509-14.
10. DONATI F, BEVAN DR. Potentiation of succinylcholine II block with isoflurane. *Anesthesiology* 1983; **58**: 552-5.
11. EGER EI. The pharmacology of isoflurane. *British Journal of Anaesthesia* 1984; **56**: 71S-99S.
12. WARREN TM, DATTA S, OSTHEIMER GW, NAULTY JS, MORRISON JA. Comparison of the maternal and fetal effects of halothane, enflurane, and isoflurane for Caesarean delivery. *Anesthesia and Analgesia* 1983; **62**: 516-20.

Low volume, high concentration block of the sciatic nerve

B. E. SMITH AND D. SIGGINS

Summary

Sciatic nerve block was performed in two groups of patients using a low power peripheral nerve stimulator to aid nerve location. In group A 1% prilocaine with felypressin was used as the local anaesthetic agent in a volume of 0.25 ml/kg body weight. In group B 3% prilocaine with felypressin was used in a volume of 0.08 ml/kg body weight (i.e. equal total drug dosages). Use of the 3% solution resulted in highly significant reductions in the mean latency for analgesia of the nerve block and in the latency and degree of motor block achieved ($p < 0.005$ in each case). The clinical value of high concentration, low volume nerve block is discussed.

Key words

Anaesthetic techniques; regional, sciatic nerve block.
Equipment; nerve stimulators.

The demonstration that greater accuracy of needle placement can be achieved by use of a low power peripheral nerve stimulator during sciatic blockade,¹ should permit the use of smaller volumes and, therefore, higher concentrations of local anaesthetic solutions. Accurate needle placement and the use of concentrated solutions should result both in a reduction of latency and in greater duration of the block. This study was undertaken to test this hypothesis in the clinical setting.

Patients and methods

Forty adult patients scheduled for either elective or emergency surgery of the lower limb were studied. Patients with arterial hypertension or known hypersensitivity to local anaesthetic agents were excluded from the study. Formal consent was obtained in all cases. All patients were premedicated with diazepam 10 mg orally approximately 2 hours pre-operatively. Patients were allocated according to a random number sequence to one of two groups. In group A sciatic block was performed using 1% prilocaine with felypressin 0.01 IU/ml using a volume of 0.25 ml/kg body weight. In group B the block was performed using 3% prilocaine with felypressin 0.03 IU/ml at a volume of 0.08 ml/kg body weight. Sciatic block was performed via the posterior approach described by Raj *et al.*² using a 22-gauge uninsulated needle. A low power peripheral nerve stimulator³ was used, as described by Smith and Allison.¹ Onset of block was specified as loss of sensation to pin-

prick in both the tibial and common peroneal nerve territories. The degree of motor block was assessed using 10-cm visual analogue scores based on both the power and degree of plantar and dorsiflexion of the foot, that ranged from power normal to power absent. Testing was performed at 3-minute intervals for pinprick and 10-minute intervals for motor block by an observer blind to the patient grouping. Any block not effective at 45 minutes was deemed to have failed and alternative anaesthetic techniques were employed. The duration of block was assessed on the basis of analgesia to pinprick as above and assessments were done at approximately 2-hourly intervals, again by an observer blind to the patient grouping. Recovery of sensation in either the tibial or peroneal nerve territory was taken as regression of the block. Similarly, any complaint of pain in the sciatic distribution was noted and this point taken as the time to recovery of the block.

Arterial blood pressure was monitored at 3-5-minute intervals throughout the period of anaesthesia and surgery, using automated oscillometry (Dinamap), and the electrocardiograph monitored continuously. The data were analysed using Wilcoxon rank sum testing or Chi-square testing (with Yates' correction) as appropriate.

Results

There were no significant differences between the two groups in respect of age, weight, sex or the duration and nature of surgery undertaken. The results for latency of

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Table 1. Latency of analgesia to pinprick.

	Group A (1%) (n = 20)	Group B (3%) (n = 20)	p
Mean (range) latency, minutes	20.7 (15-30)	8.2 (3-15)	<0.005
Number effective* at 15 minutes	5	19	<0.005

* Surgical anaesthesia produced.

Table 2. Degree of motor block produced in each group. Scores were derived from visual analogue score lines, 0 = normal power, 10 = motor block.

Time from injection, minutes	Mean (range) visual analogue score		p
	Group A (1%)	Group B (3%)	
10	1.16 (0-3.1)	3.5 (0-5.7)	<0.005
20	2.7 (0-4.8)	7.5 (1.3-10)	<0.005
30	3.61 (1.4-5.3)	9.2 (3.1-10)	<0.005

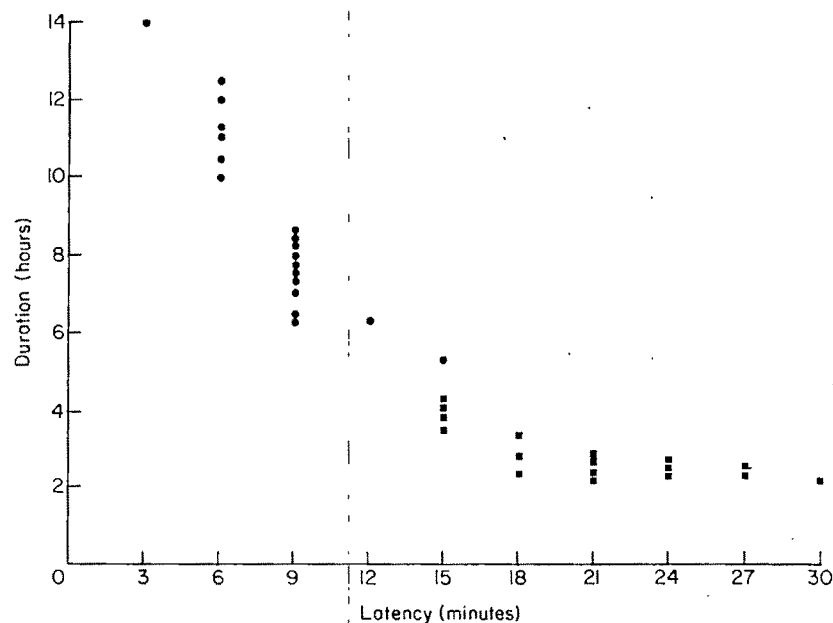


Fig. 1. Plot of the duration of analgesia against latency for both groups. ■, Group A (1%); ●, group B (3%). The three patients (two in group A, one in group B) who required posterior tibial nerve block, and the one patient in group A who required general anaesthesia, have been excluded.

analgesia to pinprick for the two groups are summarised in Table 1. The difference in mean latency was statistically significant ($p < 0.005$). The differences in mean motor block scores at 10, 20 and 30 minutes (Table 2) were all statistically significant ($p < 0.005$ in each case). The duration of analgesia to pinprick in the two groups is summarised in Table 3. The relationship between latency and duration of analgesia to pinprick is shown in Fig. 1.

Pulse rate

Mean pulse rate increased significantly in all patients during performance of the block and immediately prior to surgery, by 18 beats/minute (range 4-46) and 23 beats/minute (range 12-24), respectively, compared with the resting pulse rate (mean 82 beats/minute, range 56-108). There was no significant difference between the two groups in this respect.

Arterial blood pressure

No significant change in arterial pressure occurred in group during the performance of the block, or in the 20 minutes of the study. Mean arterial pressure minutes in group B was lower by an average of 16 in comparison to group A; this was significant at the 5% level.

Duration of surgery

The shortest surgical procedure in the series was 8 min and the longest, 3 hours 20 minutes. The shortest duration of surgical anaesthesia as assessed by pinprick was 2.1 min in group A and 5.3 hours in group B. General anaesthesia was required for completion of surgery begun under regional anaesthesia in three cases in group A, while one patient required this in group B.

Table 3. Mean duration of block as judged by analgesia to pinprick or first complaint of pain in the sciatic distribution.

	Group A (1%)	Group B (3%)	p
Mean (range) duration, hours	2.75 (2.1–4.3)	8.6 (5.3–14)	<0.005
Number pain free at 6 hours	0	15	<0.005

Combined blocks

Nineteen of the 20 blocks in group A were combined with other local nerve blocks, which included 11 femoral, eight saphenous, 12 obturator, 13 lateral cutaneous nerve of thigh and two posterior tibial nerve blocks. The maximum total dosage of prilocaine in any patient was 10.3 mg/kg. Eighteen of the 20 blocks in group B were combined with other blocks that included 12 femoral, 10 obturator, eight saphenous, 11 lateral cutaneous nerve of thigh and one posterior tibial nerve block. The total dosage of prilocaine did not exceed 10 mg/kg in any patient.

Adverse effects

No adverse effects attributable to the local anaesthetic agent were seen in any patient. In particular, there was no clinical evidence of methaemoglobinaemia in any patient. Sedation attributable to the local anaesthetic was noticeably absent.

Failed blocks

Analgesia was inadequate for surgery in three patients in group A. Analgesia was completed in two patients by the use of posterior tibial nerve blocks at the ankle, while one patient required general anaesthesia. One block in group B demonstrated inadequate analgesia which was again completed with a posterior tibial block. All four patients were excluded from the analysis of the data given in Tables 2 and 3 and from Fig. 1.

Discussion

The two main factors which determine the latency of a clinical nerve block are the accuracy of placement of the needle tip in relation to the nerve trunk, and the concentration and volume of the local anaesthetic agent used. Difficulties in accurate location of the sciatic nerve are usually overcome by infiltration of the general area of the nerve with a relatively large volume of solution, usually 15–30 ml 1% lignocaine for sensory blockade and up to 25 ml 2% lignocaine if motor block is required.⁴ The use of such volumes imposes strict limits upon the concentration of local anaesthetic agents if systemic toxicity is to be avoided. The total drug dosage that results from the use of 25 ml 2% solution is 500 mg, or approximately 7 mg/kg in a 70 kg patient. Even with the addition of adrenaline this represents the maximum recommended dosage for a healthy patient.⁵ Even with these doses latency is quoted as 30–40 minutes.⁴ Sciatic block alone is of limited value clinically and is usually combined with other nerve blocks such as femoral or saphenous block. The risk of systemic toxicity becomes considerable with such combined blocks. As the present study shows, accurate location of the sciatic nerve permits the use of small volumes of relatively concentrated solutions of local anaesthetic, which results in a significant

reduction in latency accompanied by a rapid onset and high degree of motor block. Total drug dosage can, therefore, be reduced without reduction in the efficacy of the block.^{1,2} A 70-kg patient in group B would require 5.6 ml 3% prilocaine, which represents a total dosage of 168 mg/kg body weight, less than one-quarter of the permissible dose.⁶ This results in a greater margin of safety when combined blocks are used, and also produces a more satisfactory block. The use of the 3% prilocaine solution also resulted in a greater duration of action of the block. The results shown in Table 3 should be interpreted with caution, however, since the concentration of felypressin used in the two solutions was not comparable. The 1% solution of prilocaine was prepared by dilution of the generally available 3% dental solution. Felypressin itself is not commercially available in the UK and no available solution of prilocaine, other than 3%, contains this vasoconstrictor. It would seem unlikely, however, that the difference in concentration of felypressin in the two solutions could produce such a marked difference in the duration of analgesia (2.7 hours for group A and 8.6 hours for group B).⁷ As Fig. 1 shows, the duration of action is closely related to the latency which, in turn, is related primarily to the concentration of the solution used. The prolonged duration of the block is more likely, therefore, to be the result of the concentration of local anaesthetic agent used. The addition of a vasoconstrictor would tend to increase the maximum intraneural concentration of the drug during phase 1 of the block but it would have only minimal effects upon the latency of the sensory blockade in the case of the 3% solution.⁷ Despite this, 17 of 20 patients in group B showed surgical anaesthesia within 9 minutes of injection, and 19 patients had surgical anaesthesia at 15 minutes, whereas in group A only five of 20 patients were insensitive to pinprick at 15 minutes. The rapidity of onset of analgesia following the use of the 3% solution has practical clinical significance in that it is apparent within 10 minutes from the time of injection whether the block will be adequate for surgery. The majority of group B patients reported subjective symptoms such as warmth or tingling in the foot within 5 minutes of the injection. Such rapid feedback permits the anaesthetist to re-attempt the block or to adopt alternative anaesthetic techniques earlier, thus minimising any delay in the start of surgery.

The shortest duration of any block in group B was over 5 hours and was, on average, a little over 8 hours. This makes even prolonged surgical procedures possible under a single shot block.

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References

1. SMITH BE, ALLISON A. Use of a low power peripheral nerve stimulator during sciatic blockade. *Anaesthesia* 1987; **42**: 296-8.
2. RAJ PP, PARKS RI, WATSON TD, JENKINS MT. A new single position approach to sciatic-femoral block. *Anesthesia and Analgesia* 1975; **54**: 489-93.
3. SMITH BE. Distribution of evoked paraesthesiae and effectiveness of brachial plexus block. *Anaesthesia* 1986; **41**: 1112-5.
4. LÖFSTRÖM B, ENGLESSON S. Nerve block in the region of the hip-joint. In: ERIKSSON E, ed. *Illustrated handbook in local anaesthesia*, 2nd edn. London: Lloyd-Luke, 1979: 101-10.
5. WATT MJ. The pharmacology of local anaesthetic agent LEE JA, BRYCE-SMITH R, eds. *Practical regional analgesia (A graphs in anaesthesiology, Vol. 5)*. New York: American Els 1976.
6. LUND PC. A correlation of venous blood concentration: spinal fluid concentrations of Xylocaine and Citanest d peridural analgesia. *Acta Anaesthesiologica Scandinavica* Suppl. **16**: 97-100.
7. BROMAGE PR. A comparison of the hydrochl and carbon dioxide salts of lignocaine and caine in epidural anaesthesia. *Acta Anaestologica Scandinavica* 1965; Suppl. **16**: 55-69.

Plasma concentrations of bupivacaine during extradural anaesthesia for Caesarean section

The effect of adrenaline

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Summary

The clinical effects and plasma levels associated with the use of 0.5% bupivacaine with and without the addition of 1:200 000 adrenaline (5 µg/ml) were studied in 30 patients who underwent extradural anaesthesia for elective Caesarean section. The addition of adrenaline to bupivacaine prolongs analgesia, reduces the degree of hypotension and delays its onset. Plasma bupivacaine levels were consistently lower when adrenaline was added, but this difference was significant only at 10 minutes after the initial dose. Prolonging the interval between increments seems to be a more reliable way to reduce plasma concentration than the addition of the catecholamine.

Key words

*Anaesthetic techniques; regional, extradural.
Anaesthetics, local; bupivacaine.*

There is growing interest in the use of extradural analgesia for Caesarean section and bupivacaine hydrochloride, since it is relatively long-acting and is associated with significantly less placental transfer than other local anaesthetic agents, is the most commonly used agent in the UK.¹ However, its slow onset can lead to the administration of doses in excess of requirements in an endeavour to hasten the establishment of a satisfactory block. Thompson and co-workers² showed that increasing the time interval between increments, based on assessments of sensory blockade, significantly decreased total dosage, plasma levels and side effects. Such advantages might be achieved more quickly by use of bupivacaine with adrenaline solution.³ Abboud and colleagues⁴ showed that the addition of 1:300 000 adrenaline during extradural analgesia in labour, significantly decreased the incidence of maternal hypotension and prolonged the duration of analgesia.

The present study compared the clinical effects and plasma levels associated with the use of bupivacaine 0.5% plain and with adrenaline 1:200 000 (5 µg/ml) for extradural anaesthesia for elective Caesarean delivery.

Methods

The investigation was carried out in fit, healthy women who selected extradural anaesthesia for elective Caesarean

delivery. Duration of gestation did not influence selection, but no condition was present which might jeopardise infant well-being. All gave verbal consent to be included in the study. Antacid therapy varied throughout the period of study. Approximately half of the patients in each group were given ranitidine 150 mg orally 2 hours before commencement of the extradural blockade.

Before institution of the block, which was performed in the left lateral position, all patients received a fluid preload of 1.0 litre Hartmann's solution with a further 0.5–1.0 litre during the onset of block. The intravenous infusion was set up without local anaesthesia. The extradural space was located at L₂₋₃ or L₃₋₄ using a 16-gauge Tuohy needle and Macintosh balloon. A catheter was then introduced and either plain bupivacaine 0.5% or bupivacaine 0.5% with adrenaline 1:200 000 (5 µg/ml) administered. No other local anaesthetic drug was used and the amount used for local infiltration was included in the total dose of bupivacaine. The patients were randomised as to use of adrenaline, and the anaesthetist who performed the block and the observer were both unaware of the solution used, as was the technician who measured the plasma levels.

A test dose of bupivacaine 10 mg was followed by the initial bolus of 40 mg, given in the sitting position. Further doses were given at 20-minute intervals on the basis of 1.5 ml/unblocked segment below the sixth thoracic dermatome

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(T₆), administered in a slight head-down position with the patient lying on the less blocked side. Assessments of sensory blockade were continued at 20-minute intervals in both groups and further increments given until loss of pinprick sensation reached T₆ bilaterally. The time of this occurrence from the initial administration was noted.

A 20° left lateral tilt was maintained throughout. All patients breathed 40% oxygen in air until delivery of the infant. Arterial blood pressure and heart rate were recorded by oscillonometer (Dinamap 854, Critikon) and by ECG, respectively, before institution of the block and at 3-minute intervals until birth. Hypotension, defined as a systolic pressure reading below 90 mmHg, was treated promptly with intravenous increments of ephedrine 5 mg. The greatest change in cardiovascular measurements, together with time and dosage of vasopressor administration, was recorded.

Side effects were noted when patients complained spontaneously of these. Nausea unassociated with hypotension was treated with intravenous metoclopramide. Syntocinon 5 units was given as a bolus injection at birth followed by a slow infusion of 10 units in 0.5 litres 5% dextrose.

The quality of the extradural anaesthesia was graded as excellent, satisfactory or failed; the latter required the administration of general anaesthesia. Excellent referred to those women who experienced no discomfort with minimal side effects, satisfactory to those who experienced mild discomfort, emetic or hypotensive effects that required treatment either individually or together. The time to the first intramuscular postoperative analgesic treatment was recorded and the time interval from maximum sensory block calculated. Apgar minus colour scores at 1 and 5 minutes were recorded for each baby.

Venous blood was collected from an antecubital vein of the noninfusion arm via a 16-gauge catheter fitted with a three-way tap; patency was ensured by flushing with heparinised saline. Samples were taken before and at 10-minute intervals after the administration of the first full dose of local anaesthetic into the extradural space, until the end of surgery. A maternal and umbilical venous sample was taken at birth. The samples were centrifuged and the supernatant plasma stored at -20°C until analysis. The bupivacaine was extracted from the venous plasma using ether and estimations were made using high-performance liquid

chromatography with ultraviolet detection at 220 nm. Mepivacaine was used as the internal standard. The coefficient of variation of the repeat analysis of a single sample was 5.50%. Bupivacaine was dissolved in the injection solution as bupivacaine hydrochloride monohydrate (C₁₈H₂₈N₂OHCl·H₂O) and results are given in terms of the hydrochloride salt.

Statistical analysis was carried out using analysis of variance for the plasma bupivacaine levels and independent *t*-tests for parametric data.

Results

Of 30 women in the study, 19 received plain bupivacaine 0.5% (group 1) and the remaining 11, bupivacaine 0.5% with adrenaline 5 µg/ml (group 2); the imbalance in numbers occurred despite randomisation at the point of entry to the study. Results are expressed as mean (SD).

The two groups were broadly comparable with regard to their physical characteristics and length of gestation (Table 1). Nine of the 19 patients in the non-adrenaline group and six of the 11 patients in the adrenaline group received oral ranitidine pre-operatively.

The total dose and extradural block data are shown in Table 2. There was no significant difference between the groups with regard to total dose, time to achieve maximum blockade, incidence of side effects or quality of blockade. However, the time from maximum sensory blockade until requirement for intramuscular analgesia was significantly longer in the patients who received bupivacaine with adrenaline (*p* < 0.05).

Plasma levels in both groups showed marked variation between patients, particularly in those given the adrenaline-containing solution. The mean plasma bupivacaine levels in the two groups estimated at 10-minute intervals are shown in Fig. 1. Plasma levels were higher in the patients who received plain bupivacaine but the difference between the two groups was significant only at 10 minutes (*p* < 0.04). The differences in mean maternal vein (MV) or umbilical vein (UV) plasma bupivacaine levels or the UV/MV ratio at delivery, were not significant between the two groups (Table 3).

Figure 2 shows the plasma bupivacaine levels for the nine patients who received ranitidine and those who did not.

Table 1. Physical characteristics of patients and lengths of gestation. Values expressed as mean (SD).

Group	Weight, kg	Age, years	Length of gestation, weeks
Plain bupivacaine (<i>n</i> = 19)	77 (5.6)	30 (3.4)	38 (1.1)
Bupivacaine with adrenaline (<i>n</i> = 11)	78 (6.7)	30 (2.9)	39 (1.0)

Table 2. Comparison of factors associated with extradural bupivacaine with and without adrenaline.

Group	Mean (SD) total dose, mg	Mean (SD) time to achieve maximum block, minutes	Mean (SD) time from maximum block until intramuscular analgesia, minutes	Incidence of nausea and vomiting	Use of ephedrine	Quality of block	
						Excellent	Satisfactory
Plain bupivacaine	115 (25.2)	48 (11.6)	187 (84.2)*	7	7	12	7
Bupivacaine with adrenaline	111 (13.7)	47 (8.4)	321 (70.8)*	4	5	6	5

* Significant difference (*p* < 0.05).

Table 3. Mean (SD) maternal and umbilical vein plasma concentrations at delivery following bupivacaine with and without adrenaline.

Group	Venous plasma concentration at delivery, ng/ml		UV/MV ratio
	Maternal (MV)	Umbilical (UV)	
Plain bupivacaine	924 (361.1)	318 (192.0)	0.38 (0.234)
Bupivacaine with adrenaline	807 (405.7)	231 (99.3)	0.31 (0.132)

Table 4. Control values and maximum changes in mean arterial blood pressure and heart rate during the onset of extradural blockade in the two groups. Values expressed as mean (SD).

Group	Mean blood pressure, mmHg			Heart rate, beats/minute		
	Before	After	Change, %	Before	After	Change, %
Plain bupivacaine	99 (9.9)	77 (15.1)	- 23 (13.9)	92 (13.1)	96 (29.8)	6 (31.8)
Bupivacaine with adrenaline	92 (9.2)	81 (17.9)	- 10 (26.3)	93 (18.0)	108 (20.8)	16 (35.3)

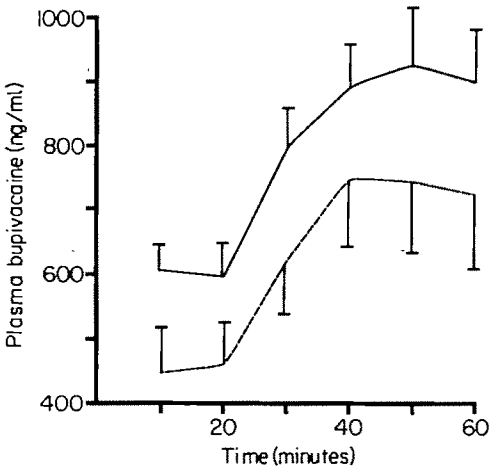


Fig. 1. Plasma bupivacaine levels (mean, SEM) during extradural analgesia for Caesarean delivery in the two groups. —, Plain bupivacaine; ----, bupivacaine with adrenaline.

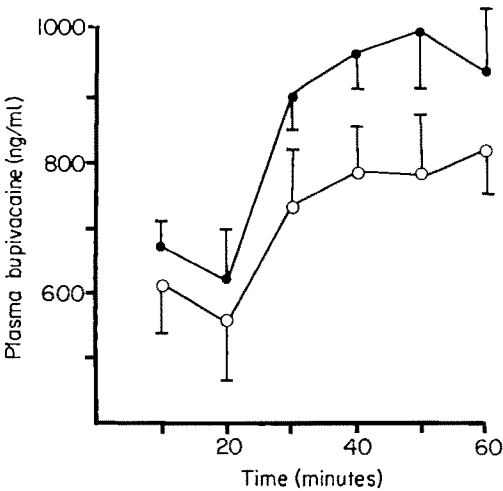


Fig. 2. Plasma bupivacaine levels (mean, SEM) during extradural analgesia for Caesarean delivery after administration of plain bupivacaine. ●, Ranitidine pretreatment (n = 9); ○, no ranitidine pretreatment.

These patients received bupivacaine without adrenaline. Those pretreated with ranitidine had higher plasma levels; the difference was significant at 40 minutes ($p < 0.05$).

The control values for mean arterial blood pressure and heart rate, together with the maximum changes in these values that occurred during the onset of the blockade, are shown in Table 4. Mean arterial pressure decreased in both groups during the onset of blockade and there was an increase in heart rate. The only change of significance was the decrease in mean arterial pressure in patients given plain bupivacaine ($p < 0.001$). The recorded decrease in systolic and diastolic arterial pressures occurred on average 23 minutes (SD 12.3) after institution of the block in the plain bupivacaine group, as compared to 42 minutes (SD 13.9) in the adrenaline group. These differ significantly at the 0.1% level. Ephedrine treatment for hypotension was required in seven patients given plain bupivacaine at 31 minutes (SD 14.9), compared to five patients at 47 minutes (SD 14.7) in the bupivacaine plus adrenaline series; these differences are not significant.

There were no significant differences in the distribution of Apgar scores in the series. These were 6.6 (range 4–7) and 6.9 (range 5–7) for the plain bupivacaine and bupivacaine with adrenaline groups, respectively. Comparative scores at 5 minutes were 7.8 and 7.9, both with a range of 7–8.

Discussion

The use of adrenaline-containing local anaesthetic solutions in obstetrics is controversial. Prolongation of analgesia and lower maternal and fetal plasma levels have been reported as the main advantages over the use of plain solutions. Reynolds *et al.*⁵ showed that the mean maternal and umbilical venous plasma concentrations of bupivacaine were significantly reduced by the addition of 1:200 000 adrenaline, but the duration of the extradural blockade was not increased. However, Abboud and colleagues⁴ reported that adrenaline prolonged analgesia without alteration of plasma levels in maternal or cord blood. The present study, carried out in non-labouring women who underwent elective Caesarean section, showed that while plasma bupiva-

caine levels were consistently lower if adrenaline was used, this was significant only at 10 minutes after the initial dose. Prolonging the interval between increments² would seem a more reliable way to reduce plasma concentration than the addition of the catecholamine. Increase in the duration of analgesia, as estimated by the time to first postoperative analgesic treatment, averaged 134 minutes in the present study, which contrasts sharply with the findings of Reynolds *et al.*⁵ who reported no increase, but agrees with those of Abboud and colleagues.⁴ These two studies were carried out in patients during labour and the differences in findings might be due to variations in uptake, distribution and elimination of drugs associated with the stages of parturition. The quality of the extradural block during the intra-operative period in our study was not affected by the addition of adrenaline; 12 of 19 patients in the plain bupivacaine group and six of 11 in the adrenaline group had excellent analgesia with a similar incidence of side effects.

The cardiovascular changes reported here differ somewhat from those reported by Bonica *et al.*⁶ These workers compared the circulatory effects of lignocaine alone and with adrenaline (5 µg/ml) and reported a greater decrease in mean arterial pressure with the latter. They suggested that this was due to β -adrenergic stimulation which, while it results in an increase in heart rate, stroke volume and cardiac output, produces a marked decrease in total peripheral resistance. Our study showed a delayed onset, a lesser degree of hypotension and a longer interval from instillation of the block to need for vasopressor treatment in patients who received bupivacaine with adrenaline. Here, however, the patients were pregnant, our comparative initial dose of bupivacaine was smaller, the total dose was administered much more slowly and intensive intravenous fluid loading was given during the initiation of the block. Abboud *et al.*⁴ in another obstetric study that compared bupivacaine with and without adrenaline, found a lower incidence of hypotension with the catecholamine and attributed this to both its β - and α -adrenergic stimulating effects.

Marx⁷ stated that the test dose should contain adrenaline so that intravascular siting of the catheter is readily recognised. Adrenaline may also have a role in the prevention or amelioration of myocardial depression associated with an inadvertent intravenous dose of bupivacaine.⁸

Bupivacaine levels in umbilical venous blood were lower in the adrenaline series but the umbilical vein/maternal vein ratios were closely similar for both groups. The slightly reduced transfer might be due in part to reduced placental blood flow, but definitive studies by Jouppila and colleagues⁹ and Albright and co-workers¹⁰ showed no significant changes in intervillous blood flow when 40–100 µg adrenaline was added to local anaesthetics for lumbar extradural analgesia.

There is justifiable anxiety about the interaction of local anaesthetics with H₂-receptor blockers,¹¹ particularly in the light of the effect of some of these on microsomal drug oxidative function^{12,13} and liver blood flow.¹⁴ The similarity in the time course of decay in plasma bupivacaine levels in patients who did and did not receive ranitidine (Fig. 2), together with the slightly higher concentration in the former group, suggests a change in volume of distribution rather than an effect on metabolism. Reduction in gastric acidity could explain this. Further study of the effect

of H₂ blockers on the disposition of bupivacaine is required.¹⁵

The addition of adrenaline to bupivacaine for extradural anaesthesia prolonged analgesia, delayed and modified the associated hypotension but reduced plasma levels only slightly. There is no doubt that its inclusion in the test dose associated with ECG monitoring will give immediate indication of intravenous administration of local anaesthetic. Nevertheless, the inclusion of a vasoconstrictor may cause decreased placental blood flow and this must be a major consideration in the presence of associated maternal hypotension.

Acknowledgments

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References

1. THOMAS J, LONG G, MOORE G, MORGAN D. Plasma protein binding and placental transfer of bupivacaine. *Clinical Pharmacology and Therapeutics* 1976; **19**: 426–34.
2. THOMPSON EM, WILSON CM, MOORE J, MCCLEAN E. Plasma bupivacaine levels associated with extradural anaesthesia for Caesarean section. *Anaesthesia* 1985; **40**: 427–32.
3. MURPHY TM, MATHER LE, STANTON-HICKS MD'A, BONICA JJ, TUCKER GT. The effects of adding adrenaline to etidocaine and lignocaine in extradural anaesthesia. I. Block characteristics and cardiovascular effects. *British Journal of Anaesthesia* 1976; **48**: 893–8.
4. ABOUD TK, SHEIK-OL-ESLAM A, YANAGI T, MURAKAWA K, COSTANDI J, ZAKARIAN M, HOFFMAN D, HAROUTUNIAN S. Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. *Anesthesia and Analgesia* 1985; **64**: 585–91.
5. REYNOLDS F, HARGROVE RL, WYMAN JB. Maternal and foetal plasma concentrations of bupivacaine after epidural block. *British Journal of Anaesthesia* 1973; **45**: 1049–53.
6. BONICA JJ, AKAMATSU TJ, BERGES PU, MORIKAWA K, KENNEDY WF. Circulatory effects of peridural block. *Anesthesiology* 1971; **34**: 514–22.
7. MARX GF. Cardiotoxicity of local anaesthetics—the plot thickens. *Anesthesiology* 1984; **60**: 3–5.
8. MOORE DL, SCURLOCK JE. Possible role of epinephrine in prevention or correction of myocardial depression associated with bupivacaine. *Anesthesia and Analgesia* 1983; **62**: 450–3.
9. JOUPPIILA R, JOUPPIILA P, KUITKA J, HOLLMEN AI. Placental blood flow during Caesarean section under lumbar extradural analgesia. *British Journal of Anaesthesia* 1978; **50**: 275–9.
10. ALBRIGHT GA, JOUPPIILA R, HOLLMEN AI, JOUPPIILA P, VIEROLA H, KOIVULA A. Epinephrine does not alter human intervillous blood flow during epidural anesthesia. *Anesthesiology* 1981; **54**: 131–5.
11. HODGKINSON R. Potential interactions between cimetidine and amide local anesthetics in obstetrics. *Anesthesiology* 1984; **60**: 508.
12. HENRY DA, MACDONALD IA, KITCHINGMAN G, BELL GD, LANGMAN MJS. Cimetidine and ranitidine: comparison of effects on hepatic drug metabolism. *British Medical Journal* 1980; **281**: 775–7.
13. FEELY J, GUY E. Lack of effect of ranitidine on the disposition of lignocaine. *British Journal of Pharmacology* 1983; **15**: 378–9.
14. FEELY J, GUY E. Ranitidine also reduces liver blood flow. *Lancet* 1982; **i**: 169.
15. WILSON CM, MOORE J, GHALLY RG, MCCLEAN E, DUNDEE JW. Plasma bupivacaine concentrations associated with extradural anaesthesia for Caesarean section: influence of pretreatment with ranitidine. *British Journal of Anaesthesia* 1986; **58**: 1330P–1P.

CASE REPORT

Respiratory disturbance during recovery from etomidate anaesthesia

C. J. R. PARKER

Summary

A case is described in which recovery from the administration of a single dose of etomidate was complicated by periodic episodes of unconsciousness, tremor and apnoea. Subsequent investigations did not reveal any evidence of neurological disease.

Key words

*Anaesthetics, intravenous; etomidate.
Ventilation; apnoea.*

Etomidate is a non-barbiturate, intravenous anaesthetic agent whose rapid breakdown by esterases suggests that it may be of value for minor surgery in outpatients.¹ Excitatory effects such as tremor and hypertonus, as well as pain on injection, are common^{1,2} and may have hindered the more widespread use of the drug. A case is reported in which recovery from a single dose of etomidate was complicated by disturbance of the central nervous system with apnoea.

Case history

A 41-year-old female, weight 78 kg, was scheduled to undergo sigmoidoscopy for the investigation of rectal pain. She had been anaesthetised uneventfully on five previous occasions, most recently 8 years ago. She had no history of epilepsy or neurological abnormality and routine clinical examination was normal. The haemoglobin concentration was 13.6 g/dl. No premedication was given, in accordance with usual practice in this day case surgery unit.

Anaesthesia was induced through an indwelling intravenous needle with etomidate 20 mg. Excitation on induction was minimal; there was some eyelid tremor but no hypertonus of trunk or limbs. Spontaneous respiration was regular and anaesthesia was maintained with a flow of 12 litres/minute, 66% nitrous oxide in oxygen delivered to a Mapleson C system. The procedure lasted 3 minutes and the rectum appeared normal. No further intravenous drugs were given and the patient regained consciousness promptly. She was able to obey commands and to name the place and her hospital ward.

About 5 minutes after recovery the patient became un-

responsive to command and to painful stimuli; the eyes rolled cranially and there was marked tremor of the eyelids. Breathing became irregular, with alternating episodes of apnoea and hyperventilation. There was little movement of the extremities, which were flaccid, and there was no incontinence. Electrocardiography at this time revealed sinus tachycardia with a rate of 126 beats/minute and arterial blood pressure was 130/80 mmHg. The lungs were manually inflated with oxygen by facemask during apnoea and the mucous membranes did not become cyanosed. Maintenance of a clear airway was easy and tracheal intubation was not performed. This state continued for about 5 minutes, when the intravenous administration of diazepam 5 mg was followed by cessation of excitatory activity, a return of regular respiration and a decrease of heart rate to 82 beats/minute. The effect of the first dose of diazepam lasted only a few minutes, however, and then the return of excitatory activity necessitated further doses to a total of 20 mg over the next 2 hours together with thiopentone 400 mg and phenytoin 500 mg given intravenously in divided doses.

Investigations at the time revealed a blood glucose level of 4.7 mmol/litre, sodium 140 mmol/litre, potassium 3.7 mmol/litre, urea 3.4 mmol/litre, calcium 2.22 mmol/litre and albumin 41 g/litre. Arterial blood analysis whilst she breathed 100% oxygen showed pH 7.39, P_{aO_2} 66 kPa and P_{aCO_2} 5.0 kPa.

Subsequent recovery was uncomplicated. The patient was discharged from hospital 5 days later and had no recall of the complications during her recovery. Examination by a neurologist revealed no abnormality. Liver function tests were normal and a VDRL test for syphilis was negative.

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An electroencephalograph performed 7 weeks later showed no specific features.

Discussion

The intravenous administration of etomidate is often preceded by opiate premedication in an attempt to reduce the high incidence of involuntary movement and hyper-tonus on induction. This was omitted in the present case but excitation during induction was not a problem. Furthermore, the omission of other medication in this patient simplifies interpretation of the events which occurred during recovery.

Early evaluations of etomidate drew attention to the occurrence of apnoea on induction in up to 40% of patients;³ this was transient and recovery was not complicated. Apparently benign myoclonus following brief anaesthesia with etomidate has been reported in the American literature.⁴ Prolonged myoclonus following anaesthesia in which a total of 350 mg etomidate was given over a period of about 4 hours, has also been reported but, in that case, return of consciousness was delayed until myoclonus was diminishing and spontaneous respiration was satisfactory throughout recovery. Myoclonus appears not to be associated with epileptiform discharges; rather, it is interpreted as the unopposed activity of subcortical systems as they recover more quickly from the depressant effects of etomidate than the cortex which normally inhibits them.⁵

There is conflicting evidence about the existence of a convulsant effect of etomidate. Etomidate has anticonvulsant activity in animal models but at doses greatly in excess of those used in man.⁶ However, recent work has shown that etomidate 0.2 mg/kg increases epileptiform activity in a proportion of epileptic patients who undergo craniotomy.^{7,8}

It seems reasonable to suppose that the events during recovery in the present case, represent an ictal response to etomidate although the features are not those of a grand mal convulsion. There was evidence of instability of the central nervous system and the effects were transiently sup-

pressed by boluses of diazepam up to a cumulative dose of 20 mg and subsequently by repeated small doses of thiopentone.

In this patient the excitatory effects began within a few minutes of induction and before significant metabolism or excretion could have occurred. However, they followed a period of consciousness during which the patient was able not only to obey commands, but also to converse and display orientation in place. The events were not regarded as benign since there was interference with the respiratory rhythm that included apnoea. Diazepam and thiopentone might have been expected to further compromise spontaneous ventilation but the respiratory disturbance was noted before any pharmacological treatment was given and the response to the drugs included a return to regular breathing.

It is concluded that recovery from anaesthesia with etomidate may be complicated by cerebral excitation that begins after recovery of consciousness, in patients with no previous or subsequent evidence of neurological disorder.

References

1. DUNDEE JW. *Intravenous anaesthetic agents. Current topics in anaesthesia, Vol. 1.* London: Arnold, 1979.
2. FRAGEN RJ, CALDWELL N, BRUNNER EA. Clinical use of etomidate for anaesthesia induction: a preliminary report. *Anaesthesia and Analgesia* 1976; **55**: 730-3.
3. MORGAN M, LUMLEY J, WHITWAM JG. Respiratory effects of etomidate. *British Journal of Anaesthesia* 1977; **49**: 233-4.
4. TASCH MD. Myoclonus on recovery from etomidate. *Anaesthesia and Analgesia* 1985; **64**: 943.
5. LAUGHLIN TP, NEWBERG LA. Prolonged myoclonus after etomidate anaesthesia. *Anaesthesia and Analgesia* 1985; **64**: 80-2.
6. ASHTON D. Diazepam, pentobarbital and D-etomidate produced increases in bicuculline seizure threshold; selective antagonism by RO 15-1788, picrotoxin and (\pm)-DMBB. *European Journal of Pharmacology* 1983; **94**: 319-25.
7. EBRAHIM ZY, DEBOER GE, LUDERS H, HAHN JF, LESSER RP. Effect of etomidate on the electroencephalogram of patients with epilepsy. *Anaesthesia and Analgesia* 1986; **65**: 1004-6.
8. GANCHER S, LAXER KD, KRIEGER W. Activation of epileptogenic activity by etomidate. *Anesthesiology* 1984; **61**: 616-8.

CASE REPORT

Fibreoptic intubation in Klippel–Feil syndrome

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Summary

A patient with Klippel–Feil syndrome who underwent abdominal surgery is presented and the anomaly reviewed. The anatomical abnormality and potentially unstable neck provide a potentially difficult tracheal intubation which was undertaken using an awake fibreoptic technique. The role of the fibrescope and the advantage of pre-operative assessment of the difficult airway are discussed.

Key words

Intubation, tracheal; difficult, fibreoptic.

Complications; Klippel–Feil.

In 1912 Klippel and Feil¹ described a patient who had shortening and limited movement of his neck, together with a low posterior hairline. Following the initial paper, Feil presented a further 13 examples² and classified the syndrome according to the site and extent of the spinal fusion as follows: Type I, extensive cervical and upper thoracic spinal fusion; Type II, one or two interspace fusions often associated with hemivertebrae and occipito-atlantal fusion; and Type III, Type I or Type II fusion with co-existing fusion in the lower thoracic or lumbar spine.

The incidence of Type II abnormalities was found to be 0.71% of 1400 Negro and Caucasian skeletons that were between the ages of 17 and 102 years, in a study from St Louis, Missouri, USA,³ and it is considered to be the most common form; C₂₋₃ and C₅₋₆ are the interspaces usually involved. It often remains unrecognised since the neck may appear normal and the patients asymptomatic until later in life, when they present due to their increased susceptibility to cervical osteo-arthritis, trauma or the complications of basilar impression, if present. The inheritance patterns suggest autosomal dominant transmission for the C₂₋₃ fusion and autosomal recessive for the C₅₋₆.⁴

Patients with Type I abnormalities appear to be 50 times less common than Type II but they are reported more frequently, probably because they tend to exhibit the classic triad and thus present a bizarre appearance.⁵ These patients are frequently disabled by birth injuries, or have major anomalies in other organ systems. Together with Type III fusions, the studies suggest an autosomal recessive inheri-

tance pattern with considerable variation in penetrance and expression.⁴

Sex distribution is unclear since some studies have shown an equal spread, some a preponderance of males and others a higher incidence amongst females.⁵⁻⁷ Age distribution ranges from discovery at birth to 70 years; the incidence declines with increasing age.

Klippel–Feil syndrome, the eponym first used in 1921 by Dubreuil-Chambardel⁸ to describe further Type I cases, refers in its present usage, to all individuals with congenital fusion of the cervical vertebrae. Recent studies have shown the classic triad to be present in only 50% of cases and that restriction of neck movement is the most common finding.^{6,9}

Feil's original classification has not proved clinically useful⁹ except in the area of genetics,^{4,6} and a more practical outlook has been proposed by some authors^{9,10} who recognised cervical spine abnormality in the form of spondylosis, hypermobility or both, complicating the fusion pattern. Patients with this potential are at high risk from spinal cord injury during the minor trauma encountered in life,^{11,12} and especially during medical manoeuvres such as laryngoscopy, tracheal intubation and operative positioning. They described three potentially unstable patterns as follows: fusion of C₂₋₃ with occipitalisation of the atlas; long fusion and abnormal occipitocervical junction; and a single open space between two fused segments. Risks of neurological damage may be due to abnormalities other than the fusion pattern, and these include occipito-

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atlantal junction abnormalities, spinal canal stenosis and scoliosis.⁹

There are a great number of other anomalies that have been reported in association with the Klippel-Feil syndrome and these may be a greater threat to patients than the obvious deformity of the neck. The most commonly associated anomaly in a series of 50 patients from Delaware, USA⁹ was scoliosis, which occurred in 60% of cases. This could be of a progressive form which required surgical arthrodesis. Renal abnormalities occurred in 35%, Sprengel's deformity in 30%, deafness in 30%, synkinesia (mirror movements) in 20% and congenital heart disease in 14%, of which the most common variant was ventricular septal defect.¹³ Less common associations were ptosis, lateral rectus palsy, facial nerve palsy and upper extremity anomalies. Another study¹⁴ has put the incidence of genitourinary abnormalities as high as 64% and implicated the close embryological association between the pronephros and developing cervical spine. Other bony abnormalities such as hemivertebrae and malformed and cervical ribs, are common in Klippel-Feil syndrome. A high incidence of cleft palate seems to occur in the Klippel-Feil syndrome⁵ and other malformations of the skull and mandible have been reported.¹⁵

Case history

The patient was a 50-year-old Caucasian female who was referred for pre-anaesthetic assessment with a diagnosis of cholelithiasis. She gave an 8-month history of right hypochondrial pain and the presence of gall stones had been confirmed by ultrasound. A cholecystectomy was planned.

She had no significant past medical history but her father and one of her three children were diabetic. There was no family history of any congenital abnormalities. She had no neurological symptoms or evidence, on questioning, of cardiovascular or respiratory insufficiency.

Physical examination revealed a short, stocky female with an obvious deformity of the neck and a low posterior hairline, as shown in Fig. 1. The neck was fixed with



Fig. 1. Side view of patient.

virtually no movement in any axis, the larynx appeared high and was difficult to palpate due to thickened skin and soft tissue that overlay it. The cricothyroid space could not be identified reliably. Mouth opening was normal and her few teeth were in reasonable condition. There was no evidence of restricted movement of the lower thoracic or

lumbar spine. Examination of the cardiovascular system was unremarkable and the lung zones were clear on auscultation. Expansion was reduced on the left side of her chest although air entry was good and a spiograph (Vitalograph) showed a reasonable forced vital capacity of 1760 ml with an FVC:FEV₁ of 85%. An electrocardiogram was normal, as were haemoglobin, urea and electrolyte estimations. A chest X ray showed a normal heart size but deformity of the ribs on the left side, together with a left cervical rib. No lung lesions were seen. A full neurological examination revealed no abnormality and, in particular, there were no signs of nerve entrapment. Ultrasound of the abdomen confirmed gall stones but was otherwise normal. Specifically, the renal outlines and upper urinary tracts appeared normal. Cervical X rays showed a block fusion of the whole cervical and upper thoracic spine, and fusion of the dorsal spinous processes into a solid mass. The area of the cervico-occipital junction was abnormal, as shown in Fig. 2.

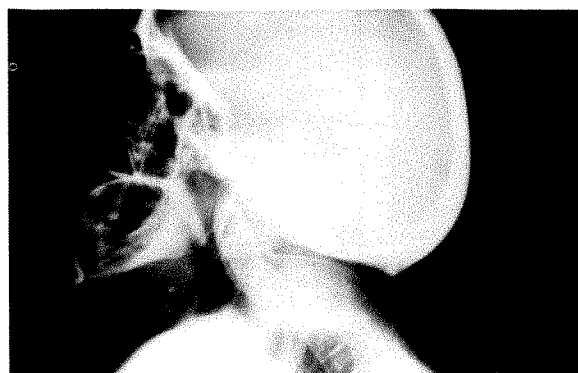


Fig. 2. Area of cervico-occipital junction.

It was decided to assess the patient's airway prior to admission and this was done using a fibreoptic endoscope (Olympus BNF Rhinolaryngo fibrescope LB) as an outpatient procedure with an unsedated patient. The path of the scope was prepared using 10% plain lignocaine spray nasally and orally, from a metered dose dispenser. When this was effective, oral laryngoscopy revealed an epiglottis that was horizontal and difficult to see beyond. The fibrescope was now gently advanced along the right nasal passage which was clear and, once the curve into the pharynx had been negotiated, the epiglottis was visible high and anterior in the neck. It was possible to manoeuvre the scope around the epiglottis, near to the vocal cords, with difficulty. It was therefore decided to perform nasal intubation under fibreoptic control prior to surgery, and to allow the maximum time for manoeuvre; this would be done with the patient awake. Informed consent was granted.

The patient was admitted to the ward the day prior to surgery and she was started on antithrombotic prophylaxis (subcutaneous heparin 5000 IU twice daily). Premedication was with temazepam 30 mg and hyoscine 0.6 mg orally 2 hours prior to surgery. The patient was placed directly on the operating table and an intravenous cannula inserted into a suitable forearm vein under local anaesthesia. The patient's head, neck and shoulders were stabilised in a comfortable position, using a large evacuating pillow which remained as a rigid support until the patient awoke at the

end of the operation. The patient's nose and pharynx were again prepared using a metered dose of 10% plain lignocaine and, after 5 mg intravenous midazolam, the instrument was passed and lignocaine 10% sprayed under direct vision, via a small nylon catheter, onto and through the vocal cords. A well-greased and warmed 7.00 mm cuffed tracheal tube (Portex), cut to a length estimated from the lateral cervical X ray, was then threaded over the fibroscope which was introduced into the right nasal passage and both tube and scope were advanced to negotiate the corner into the pharynx. The scope was then manoeuvred so that its tip passed through the cords, which elicited a slight cough from the patient. The tube was then passed into the trachea using the scope as a guide. The position of the tube was checked visually by reference to the carina, and by auscultation. Anaesthesia was then induced using thiopentone 250 mg, droperidol 2.5 mg, vecuronium 5 mg and fentanyl 150 μ g. Intermittent positive pressure ventilation with oxygen 33% and nitrous oxide 67% was established via a Penlon Nuffield 200 series ventilator and the fresh gas flow adjusted to maintain normocapnia as measured at the catheter mount (Datex Normocap). Inflation pressures were normal. The 70-minute operation, performed via a Kocher's incision, was uneventful and anaesthesia was maintained with further droperidol 2.5 mg, fentanyl 100 μ g and vecuronium 5 mg in divided doses.

At the end of surgery, intercostal blocks were performed on the right, from T₈₋₁₁, using 16 ml 0.5% bupivacaine with 1:200 000 adrenaline. Residual neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrronium 0.6 mg and the tracheal tube removed after the resumption of spontaneous ventilation and the return of good muscle tone. The postoperative course was smooth and, on the following day, she had no recall of the intubation procedure. She was discharged home on the fourth postoperative day.

Discussion

Upper abdominal incisions are generally unsuitable for local anaesthesia and the currently accepted standard of care is a relaxant technique with tracheal intubation and controlled ventilation of the lungs. This requires control of the airway and, therefore, the feasibility of intubation becomes of paramount importance. In an elective surgical case there is ample time for assessment of the various methods of approach, should there be any cause for concern.

Our patient was a typical Klippel-Feil Type I in the original classification, or Type 2 in the later classification, and displayed the classic triad. She therefore had a potentially unstable cervical spine and abnormal atlanto-occipital junction but had no other demonstrable pathology apart from rib abnormalities on the left side. Intravenous pycelography has been recommended in cases of Klippel-Feil syndrome because of the high incidence of renal abnormalities,¹⁴ but it was decided not to perform this in view of the patient's age, health, normal abdominal ultrasound and other findings.

The need for care with the occipito-cervical junction necessitated provision of rigid support for the patient's head, neck and shoulders before loss of muscle tone and prior to an atraumatic intubation. The feasibility of an awake, nasal, fiberoptic intubation as an outpatient under

local analgesia had been assessed. This gave useful information concerning the anatomy and condition of the nares, pharynx and position of the laryngeal opening. A review article¹⁶ has suggested that the flexible fibroscope should be used much more as a routine part of peri-operative assessment of patients, especially those suspected to have upper or lower airway pathology, or distorted anatomy from whatever cause. It has also been suggested that any anatomical problem that makes the success of direct laryngoscopy doubtful, is an indication for fiberoptic intubation.¹⁷

The best conditions are found in awake patients since they can assist in clearing their own secretions, phonating or panting. The nasal route is preferred since the tongue is less likely to interfere and the patient cannot bite down. If the patient is first anaesthetised, difficulty can be experienced with both clearing the secretions and ventilation, should any problem be encountered with intubation. For these reasons, fiberoptic intubation is rarely helpful in an emergency. However, on these occasions it can be valuable in assessment of the compromised airway, and in tube positioning.¹⁶

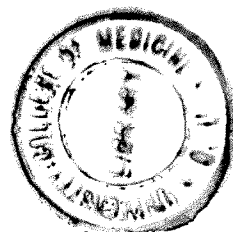
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References

1. KLIPPEL M, FEIL A. Un cas d'absence des vertèbres cervicales avec cage thoracique remontant jusqu'à la base du crâne (cage thoracique cervicale). *Nouvelle Iconographie de la Salpêtrière* 1912; **25**: 223-50.
2. FEIL A. L'absence et la diminution des vertèbres cervicales (étude clinique et pathologique). Le syndrome de réduction numérique cervicale. Thesis, Paris, 1919.
3. BROWN MW, TEMPLETON AW, HODGES FJ. The incidence of acquired and congenital fusions in the cervical spine. *American Journal of Roentgenology, Radiotherapy and Nuclear Medicine* 1964; **92**: 1255-9.
4. GUNDERSON CH, GREENSPAN RH, GLAZER GH, LUBS HA. The Klippel-Feil syndrome; genetic and clinical reevaluation of cervical fusion. *Medicine* 1967; **46**: 491-512.
5. HELMI C, PRUZANSKY S. Craniofacial and extracranial malformation in the Klippel-Feil syndrome. *Cleft Palate Journal* 1980; **17**: 65-88.
6. GRAY SW, ROMAINE CB, SKANDALAKIS JE. Congenital fusion of the cervical vertebrae. *Surgery, Gynecology and Obstetrics* 1964; **118**: 373-85.
7. NOBLE TP, FRAWLEY JM. The Klippel-Feil syndrome. *Annals of Surgery* 1925; **82**: 728-34.
8. DUBREUIL-CHAMBARDEL L. Les hommes sans cou. *Presse Medicale* 1921; **29**: 353-5.
9. HENSINGER RN, MAC EWEN GD. Congenital anomalies of the spine. In: ROTHMAN RH, SIMBONE FA, eds. *The spine*. Philadelphia: W.B. Saunders, 1982: 216-33.
10. McRAE DL. Bony abnormalities in the region of the foramen magnum: correlation of the anatomical and neurological findings. *Acta Radiologica* 1953; **40**: 335-54.
11. ELSTER AD. Quadriplegia after minor trauma in the Klippel-Feil syndrome. *Journal of Bone and Joint Surgery* 1984; **66A**: 1473-4.
12. NAGIB MG, MAXWELL RA, CHOU SN. Identification and management of high-risk patients with Klippel-Feil syndrome. *Journal of Neurosurgery* 1984; **61**: 523-30.

13. MORRISON SDG, PERRY LW, SCOTT LP. Congenital brevicolis (Klippel-Feil syndrome) and cardiovascular anomalies. *American Journal of Diseases of Children* 1968; **115**: 614-20.
14. MOORE WB, MATTHEWS TJ, RABINOWITZ R. Genitourinary anomalies associated with Klippel-Feil syndrome. *Journal of Bone and Joint Surgery* 1975; **57A**: 355-7.
15. LAWRENCE TM, McCLATCHEY KD, FONSECA RJ. Congenital duplication of mandibular rami in Klippel-Feil syndrome. *Journal of Oral Medicine* 1985; **40**: 120-2.
16. WATSON CB. Fibreoptic bronchoscopy for anaesthesia. *Anaesthesiology Review* 1982; **9**: 17-26.
17. MULDER DS, WALLACE DH, WOODHOUSE FM. The use of the fibreoptic bronchoscope to facilitate endotracheal intubation following head and neck trauma. *Journal of Trauma* 1975; **15**: 638-40.



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CASE REPORT

Isoflurane and primary pulmonary hypertension

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Summary

Primary pulmonary hypertension is a rare and fatal disease. These patients represent an anaesthetic challenge because of the high mortality associated with the marked intra-operative increase in pulmonary vascular resistance and right ventricular decompensation. This is a first case report which demonstrates the safe and beneficial effects of isoflurane in lowering pulmonary arterial pressure and pulmonary vascular resistance in such a patient for a short surgical procedure. The anaesthetic considerations in these patients are discussed.

Key words

Anaesthetics, volatile; isoflurane.

Blood pressure; pulmonary hypertension.

Primary pulmonary hypertension is a rare disease of the pulmonary vasculature. It can be diagnosed only by exclusion of other causes, especially recurrent pulmonary emboli, atrial septal defect, mitral stenosis and vasculitis. The disease largely affects young women and usually runs a rapidly fatal course. Anaesthetic management of patients with elevated pulmonary vascular resistance (PVR) represents a complex problem since intra-operative increases in PVR and, thus, right ventricular decompensation, carry a high mortality.^{1–3} The effect of isoflurane on pulmonary haemodynamics in such patients has not been documented. This report demonstrates the successful use and possible beneficial effects of isoflurane on pulmonary haemodynamics in a patient with primary pulmonary hypertension.

Case history

A 25-year-old male ski instructor was admitted to hospital for a diagnostic open lung biopsy. He was previously healthy and fit with no known allergies. He was a non-smoker and a social drinker.

One year prior to admission, he noticed increasing fatigue and a progressive deterioration in exercise tolerance. He complained of a nonproductive cough. No haemoptysis, presyncope, ankle swelling or vasculitis were noted. Five months prior to admission, he was admitted to another hospital for investigation.

Electrocardiography and echocardiography demonstrated right ventricular hypertrophy with a normal ejection

fraction. Chest X ray indicated multiple pulmonary infiltrates but pulmonary angiography failed to confirm pulmonary embolism. Pulmonary artery catheterisation showed equalisation of pulmonary artery pressure (PAP) and systemic blood pressure. He was later discharged on therapy with nifedipine and warfarin and a referral for open lung biopsy was made.

On this admission, he was short of breath on walking about one-half to three-quarters of a mile or two flights of stairs, with retrosternal heaviness. Other functional inquiry was negative. Pre-operative differential diagnosis included primary pulmonary hypertension, pulmonary veno-occlusive disease or pulmonary vasculitis.

Physical examination revealed a healthy-looking 75 kg man. There was no evidence of pallor, cyanosis, clubbing, jaundice, adenopathy or vasculitis. Vital signs including temperature were normal. Cardiovascular examination revealed a normal jugular venous pressure, positive right ventricular heave and S₄, with prominent P₂ and narrowly split S₂. Liver span was 7 cm below costal margin and nonpulsatile. Examination of other systems including chest, neurological and musculoskeletal examination was unremarkable.

Pre-operative investigation showed a normal blood count, erythrocyte sedimentation rate, serum creatinine, urea, electrolytes, total protein, albumin and calcium. The patient was anticoagulated with prolonged prothrombin and partial thromboplastin times. Arterial blood gases were pH 7.45, PaCO₂ 4.4 kPa, PaO₂ 12.2 kPa, bicarbonate 23

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Table 1. Comparison of cardiovascular and pulmonary haemodynamic parameters during isoflurane-oxygen anaesthesia in a patient with primary pulmonary hypertension.

	Pre-induction	Postinduction	Maintenance	Pre-extubation	Postextubation
SaO ₂ (%)	99	100	100	100	100
Pe'CO ₂ (kPa)	—	3.7	4.0	4.0	—
BP (mmHg)	140/60	100/40	120/50	130/50	190/70
BP (mmHg)	87	60	73	77	110
HR (beats/minute)	100	70	70	100	100
CVP (mmHg)	25	20	12	25	30
SVR (dyn/sec/cm ⁵)	708	864	574	800	—
RVP (mmHg)	160/3	—	—	—	—
PAP (mmHg)	163/68	107/66	98/62	106/69	190/78
PAP (mmHg)	99	80	76	81	115
PCWP (mmHg)	68	—	60	—	—
CO (litres/minute)	7.0	3.7	8.5	5.2	—
PVR (dyn/sec/cm ⁵)	354	302*	141	185*	—

* PADP assumed to be the downstream pressure in calculation of PVR. SaO₂, Oxygen saturation; Pe'CO₂, end tidal carbon dioxide; BP, arterial blood pressure; HR, heart rate; CVP, central venous pressure; SVR, systemic vascular resistance; RVP, right ventricular pressure; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CO, cardiac output; PVR, pulmonary vascular resistance.

mmol/litre and oxygen saturation 97% in room air. The electrocardiogram indicated marked right axis deviation of 130° and right ventricular hypertrophy. Chest X ray was clear with prominent pulmonary arteries. Pulmonary function testing showed slightly increased lung volume with total lung capacity 7 litres, functional residual capacity 4 litres, vital capacity (VC) 5.3 litres, residual volume 2.4 litres, forced expiratory volume in 1 second 3.8 litres, FEV₁/FVC ratio 91% and maximum expired flow at 25% VC (V₂₅) 1.3 litres/second. Airway resistance and diffusion were normal with a small increase in flow rates after bronchodilation.

The patient was premedicated with his regular dose of nifedipine 20 mg and diazepam 10 mg orally on the morning of surgery. Two units of fresh frozen plasma were transfused and repeat coagulation tests were normal before the left radial arterial and right internal jugular pulmonary artery catheters (Swan-Ganz thermodilution catheter No. 7.5F, VIP™) were inserted. The patient was sedated with fentanyl 100 µg supplemented with 40% oxygen. Pre-induction haemodynamic variables were recorded. Cardiac output was measured by the thermodilution technique with 10 ml injected volume at room temperature, with a cardiac output computer (Edwards Laboratory 9520). A mean of three measurements was recorded. Additional intra-operative monitors included electrocardiogram, oesophageal stethoscope and temperature probe, peripheral nerve stimulator, pulse oximeter (Ohmeda Biox III) and end tidal carbon dioxide monitor (Datascop Accucap). Pulmonary artery and arterial pressures were transduced (Datascop 2001) and calibrated with a known pressure manometer.

Induction of anaesthesia involved pre-oxygenation with 100% oxygen and the intravenous administration of lignocaine 80 mg, fentanyl 100 µg, sodium thiopentone 250 mg, atracurium 4 mg and suxamethonium 120 mg. Tracheal intubation with a cuffed Portex single lumen tracheal tube was atraumatic. Postinduction data were recorded before surgical stimulation, 5 minutes after induction, while anaesthesia was maintained with 100% oxygen, isoflurane 0.5% and atracurium 15 mg using controlled ventilation. Maintenance data were recorded 10 minutes after surgery began, when anaesthesia was maintained with 100% oxygen and isoflurane 1%. The duration of surgery was approximately 60 minutes.

Cardiovascular and pulmonary haemodynamic variables are compared in Table 1. This shows that under conditions of controlled end tidal carbon dioxide and oxygen saturation, isoflurane when used during maintenance of anaesthesia contributed to a marked decrease in PAP and in PVR. Intra-operative arterial blood gases were pH 7.46, PaCO₂ 4.6 kPa, PaO₂ 68.2 kPa, bicarbonate 24 mmol/litre, oxygen saturation 99% on FiO₂ 1.0. Pre-extubation data were recorded at the end of the procedure, after Isoflurane was discontinued for 5 minutes and the patient's lungs were still ventilated with 100% oxygen. Neuromuscular blockade was then reversed with edrophonium 50 mg and atropine 0.6 mg. The trachea was extubated when the patient was awake in the operating room. The PAP became raised again postoperatively. Postextubation data were recorded in the recovery room and the pulmonary artery catheter was withdrawn because the waveform was not properly transduced in the wedging position. Postoperative arterial blood gases were pH 7.43, PaCO₂ 5.1 kPa, PaO₂ 10.6 kPa, bicarbonate 26 mmol/litre, oxygen saturation 96% on FiO₂ 0.4.

The patient made an uneventful recovery. Pathological diagnosis was primary pulmonary hypertension with medial hypertrophy, intimal thickening and irreversible plexogenic arteriopathy. There was no evidence of emboli or vasculitis.

Discussion

Primary pulmonary hypertension is a rare disease of unknown aetiology with two essential features: elevated PVR and PAP, and no identifiable pulmonary or cardiovascular abnormality that might cause secondary pulmonary hypertension. It usually occurs in young women (80%) of age 20–40 years.^{4,5} The prognosis is extremely poor if right heart failure occurs.⁶ A familial form is occasionally seen. Raynaud's phenomenon presents in one-third of cases. The natural history is a steady downhill course; death usually occurs within 5 years.⁴

The pathophysiological sequelae of pulmonary hypertension involve mainly the cardiovascular and pulmonary systems.³ The anaesthetic management of patients with significantly elevated PVR includes pre-operative assessment of the degree of pulmonary hypertension and right and left ventricular reserve, and of the responsiveness of

the pulmonary vasculature to pharmacological vasodilatation.⁷ Monitoring should include a pulmonary artery catheter so that marked increases in PVR and right ventricular decompensation can be avoided while cardiac output and coronary perfusion pressure are maintained.

Factors that increase PVR and must be avoided during anaesthesia include hypoxia, acidosis, hypercapnia, hypothermia, extremes in lung volume, positive end expiratory pressure, hyperviscosity, agitation, alpha-adrenergic stimulation and endogenous vaso-active substances, e.g. catecholamines and histamine.³

The reported effects of anaesthetic agents on PVR have been scanty.³ Of the intravenous agents, the barbiturates lower PVR and PAP only in very high doses; the effect of ketamine is controversial; narcotics have minimal direct effect, while no good data exist for muscle relaxants. With respect to inhalational agents, current studies suggest that PVR increases significantly with nitrous oxide, especially in patients with pre-existing pulmonary hypertension.⁸ No data are available for the effect of halothane, enflurane or isoflurane on right ventricular overloaded patients.

Isoflurane-induced hypotension in humans was associated with minimal pulmonary haemodynamic derangement in patients free of cardiovascular and pulmonary disease.⁹ Isoflurane was found to have no effect on pulmonary haemodynamics in geriatric patients¹⁰ during controlled ventilation with constant P_{aCO_2} ; however, nitrous oxide, an agent that elevates PVR, was used in the study.

In this case, isoflurane appeared to be beneficial in lowering PVR and PAP and, thus, improved cardiac output in a patient with primary pulmonary hypertension. Baseline data (pre-induction) indicated that the patient had severely elevated PAP (163/68 mmHg) with a mean PAP of 99 mmHg that exceeded his mean systemic blood pressure of 87 mmHg. There was no evidence of right ventricular failure (160/3 mmHg) yet pulmonary capillary wedge pressure (PCWP) was 68 mmHg which was similar to the pulmonary artery diastolic pressure (PADP). This wedge pressure almost certainly does not accurately reflect the left ventricular end diastolic pressure or volume because the pulmonary vasoconstriction or obstruction is so severe.¹¹ Direct left atrial pressure monitoring was not feasible in our case; therefore, PCWP was used in our calculation of PVR. The error of using this high PCWP as the downstream pressure in the calculation of perfusion pressure will only underestimate the effect of isoflurane on PVR. Because the risk of pulmonary vessel perforation is high in patients with pulmonary hypertension,¹² we elected to wedge the pulmonary artery catheter only once during the maintenance of anaesthesia with isoflurane and there was no change. Otherwise, the PADP was assumed to be the downstream pressure in the haemodynamic calculation during the postinduction and pre-extubation period.

After induction, once isoflurane was added and under constant end tidal carbon dioxide and oxygen saturation, there was a gradual trend toward reversal of the pulmonary pressure versus the systemic pressure gradient, with a decrease in both. When compared with pre-induction baseline

variables, isoflurane 1% with 100% oxygen and atracurium caused a 60% decrease in PVR accompanied by a 24% decrease in PAP, a 19% decrease in SVR accompanied by a 17% decrease in arterial blood pressure, and an increase in cardiac output of 21%. At the end of surgery when isoflurane was discontinued, the haemodynamic gradients changed in the opposite direction, during which time the patient was still paralysed and his lungs ventilated with 100% oxygen. There is little question in our minds that isoflurane resulted in haemodynamic improvement after induction.

In summary, isoflurane markedly lowered pulmonary artery pressure and pulmonary vascular resistance in a patient with primary pulmonary hypertension. The effect of isoflurane on pulmonary haemodynamics was shown to be safe and beneficial when other factors that are known to elevate PVR are avoided and cardiac output and coronary perfusion are maintained.

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References

1. DAVIES MJ, BEAVIS RE. Epidural anaesthesia for vascular surgery in a patient with primary pulmonary hypertension. *Anaesthesia and Intensive Care* 1984; **12**: 165-76.
2. NELSON DM, MAIN E, CRAFT W, AHUMADA GG. Peripartum heart failure due to primary pulmonary hypertension. *Obstetrics and Gynecology* 1983; **62**: 58S-63S.
3. BURROWS FA, KLINCK JR, RABINOVITCH M, BOHN DJ. Pulmonary hypertension in children: perioperative management. *Canadian Anaesthetists' Society Journal* 1986; **33**: 606-28.
4. FISHMAN AP, PIETRA GG. Primary pulmonary hypertension. *Annual Review of Medicine* 1980; **31**: 421-31.
5. PITTMAN DE. Primary pulmonary hypertension. Case report and discussion of the literature. *Angiology* 1979; **30**: 756-67.
6. MCCAFFREY RM, DUNN LJ. Primary pulmonary hypertension in pregnancy. *Obstetrical and Gynecological Survey* 1964; **19**: 567-91.
7. REEVES JT, GROVES BM, TURKEVICH D. The case for treatment of selected patients with primary pulmonary hypertension. *American Review of Respiratory Diseases* 1986; **124**: 342-6.
8. SCHULTE-SASSE U, HESS W, TARNOW J. Pulmonary vascular responses to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology* 1982; **57**: 9-13.
9. NICHOLAS JF, LAM AM. Isoflurane-induced hypotension does not cause impairment in pulmonary gas exchange. *Canadian Anaesthetists' Society Journal* 1984; **31**: 352-8.
10. TARNOW J, BRÜCKNEER JB, EBERLEIN HJ, HESS W, PATSCHKE D. Haemodynamics and myocardial oxygen consumption during isoflurane anaesthesia in geriatric patients. *British Journal of Anaesthesia* 1976; **48**: 669-75.
11. LEVIN RI, GLASSMAN E. Left atrial-pulmonary artery wedge pressure relation: effect of elevated pulmonary vascular resistance. *American Journal of Cardiology* 1985; **55**: 856-7.
12. KRANTZ EM, VILJOEN JF. Haemoptysis following insertion of a Swan-Ganz catheter. *British Journal of Anaesthesia* 1979; **51**: 457-9.

CASE REPORT

A new technique for sleeve resection and major bronchial resection using twin catheters and high frequency jet ventilation

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Summary

A new anaesthetic technique that uses two catheters combined with high frequency jet ventilation for sleeve resection of the major bronchus and carina is described. The advantages and disadvantages are discussed and compared with other techniques.

Key words

Anaesthetics, intravenous; ketamine.

Ventilation; high frequency jet.

Sleeve resection of bronchial tumours, especially those that involve the carina, poses difficulties for both the surgeon and the anaesthetist. These include impairment of exchange during anaesthesia and the development of postoperative atelectasis as a result of bleeding into the distal part of the bronchus. The anaesthetic technique employed may also restrict surgical access.

Conventional anaesthesia for this procedure includes the use of a double lumen bronchial tube, with one lung ventilation during the resection.¹ However, this does not always prevent blood or debris soiling the distal part of the bronchus. If the resection involves the tracheal bifurcation, this method becomes very hazardous because of the risk of damage to the bronchial tube and consequent disruption of ventilation. The use of a special tube with a double cuff has been suggested in an attempt to overcome this problem.²

An alternative technique that uses a narrow, single lumen tracheal tube was described by Barclay *et al.*³ The tube is passed into the trachea and a sterile bronchial blocker is inserted from the surgical field when the bronchus is opened. The blocker is removed and the tracheal tube passed into the other bronchus during suturing of the anastomosis. However, this impedes surgical access and may cause difficulty in securing the anastomosis.

Insufflation of oxygen through a catheter located in the bronchus has been recommended⁴ but this technique does not overcome the distal escape of blood or debris into the bronchus and can result in hypoxia and hypercapnia.

Ventilation of each lung using an injector through a single catheter has been used successfully to ventilate the

lung opposite to the side of the resection,⁵ and both lungs until the time of reconstruction. However, high frequency jet ventilation (HFJV) with a catheter inserted into each main bronchus might control ventilation and gas exchange more satisfactorily. Fine bore catheters positioned with their tips distal to the resection might not only assist the escape of blood or debris⁶ but might also provide an undisturbed operating field and thus facilitate the reconstruction.

Case history

The patient was a 69-year-old man who presented initially with a history of haemoptysis for one year. Bronchoscopy had revealed a tumour in his right main bronchus; this had been removed locally and was found by histology to be a fibrous histiocytoma. He now had further haemoptysis, and bronchoscopy showed recurrence of the tumour proximal to the branch of the right upper lobe bronchus, and that the carina was involved. A decision was taken to perform a sleeve resection of his right major bronchus.

He was a slightly overweight man with a history of hypertension and chronic obstructive airways disease. No abnormalities of the cardiovascular or respiratory systems were detected on physical examination. Electrocardiography (ECG) showed generalised T-wave inversion with left bundle branch block. His chest X ray appeared normal and pre-operative arterial blood gas analysis was within the normal range. Pulmonary function tests were slightly below expected values. His medication consisted of methyl-dopa and Hygroton-K for hypertension, with prednisone and a salbutamol inhaler for respiratory symptoms.

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Anaesthetic technique

The patient was started on digitalis 0.25 mg orally before operation. Premedication was with hydrocortisone 100 mg, morphine 10 mg and atropine 0.6 mg intramuscularly. Anaesthesia was induced with intravenous Diazemuls 10 mg and ketamine 170 mg (2 mg/kg) followed by a ketamine infusion (4 mg/kg/hour) for maintenance. Neuromuscular blockade was achieved with pancuronium 6 mg (0.1 mg/kg). Bronchoscopy was performed to ascertain the size of the tumour and then a 9-mm Portex gas monitoring tracheal tube was introduced. HFJV was provided through the gas monitoring lumen using an Acutronic MK800 ventilator. ECG, arterial pressure and inspired oxygen concentration were monitored and frequent arterial blood gas analyses undertaken. The initial ventilator settings were driving pressure 130 kPa, rate 100 breaths/minute. This resulted in the following measurements: F_{IO_2} 0.58, P_{aO_2} 31.8 kPa, P_{aCO_2} 3.9 kPa. A small dose of phentolamine (2.5 mg) was given approximately 30 minutes after induction of anaesthesia to control hypertension.

When surgical access had been achieved through a sternal split, two lengths of fine tubing (Bentley pressure manometer lines 80 cm \times 3 mm) were passed through the tracheal tube and guided by the surgeons into each of the major bronchi. Their proximal ends were connected via a Y-piece to the jet ventilator and ventilation was continued through these catheters. The right upper lobe was ventilated inadequately and subsequently collapsed, with a decrease in P_{aO_2} and an increase in P_{aCO_2} (Table 1); the catheter tip was presumably beyond the opening of the upper lobe bronchus. The remainder of the right lung was seen to be well ventilated when the right main bronchus was opened but, as surgery continued, retraction of the right lower lobe caused it to collapse and there was a further deterioration in P_{aO_2} and P_{aCO_2} . The lower lobe re-expanded when retraction was discontinued. The surgery was completed without difficulty; HFJV was re-instituted through the gas monitoring port of the tracheal tube and the catheters were removed. The blood gases rapidly returned to their initial values and the remainder of the case was uneventful. The ketamine infusion was discontinued and, following administration of neostigmine and atropine, the trachea was extubated when spontaneous respiration was deemed to be satisfactory. The patient was taken to the recovery ward and later transferred to the intensive care unit for observation. He developed hypercapnia due to deterioration in his pre-existing lung condition and mechanical ventilation was required for 48 hours. The postoperative course was further complicated by atrial fibrillation which was unresponsive to digoxin and required verapamil. He was discharged home 16 days after surgery and has had no further medical problems.

Table 1. Arterial blood gases during surgery.

	F_{IO_2}	P_{aO_2} (kPa)	P_{aCO_2} (kPa)
Before surgery	0.58	31.8	3.9
Before catheter ventilation	0.75	19.5	5.3
Initial catheter ventilation	0.77	10.8	6.7
Collapse of right lower lobe	0.85	7.9	8.2
After re-expansion	0.80	12.2	6.7
Catheters removed, normal HFJV	0.60	31.6	5.7

Discussion

The double catheter technique proved to be an improvement over one lung ventilation using a double lumen tracheal tube, in that it provided unhurried, good surgical access without undue hypoxia or hypercarbia. However, a number of factors require comment.

Inhalational anaesthesia is not practical with HFJV and an intravenous anaesthetic technique must therefore be used. The practice in this unit is to use a ketamine infusion and this has been described elsewhere.⁷

From previous experience, we had anticipated the problem of the catheters being too short;⁸ the catheters used were lengths of tubing employed normally to extend intra-arterial lines. However, the tubes tended to migrate back into the trachea, particularly on the right side. In addition, care was needed to prevent collapse of the right upper lobe. Repositioning the tube under direct vision by the surgeons allowed the upper lobe to re-expand. The collapse of the right lower lobe could have been avoided if less enthusiastic retraction had been employed.

Complications due to escape of blood or debris into the distal part of the bronchus were not encountered, since the surgeon could use suction under direct vision and jet ventilation tended to expel foreign material from the distal bronchus.

Clarkson and Davies⁶ reported barotrauma caused by a catheter which impacted in a small bronchus. However, this complication can be avoided easily by careful positioning of the catheter tip.

We feel that the technique of HFJV through a double catheter system has much to recommend it for bronchial sleeve resection and is worthy of further study.

Addendum

Since this paper was prepared, the technique has been used on a second occasion. The patient was a young female with a cylindroma of the tracheal wall 2 cm above the carina. The technique was similar except that a propofol infusion was used for anaesthesia.

References

1. GOTHARD JWW, BRANTHWAITE MA. *Anaesthesia for thoracic surgery*. Oxford: Blackwell Scientific, 1982: 116-7.
2. KAPLAN JA, ed. *Thoracic anaesthesia*. New York: Churchill Livingstone, 1983.
3. BARCLAY RS, MCSWAN N, WELSH TM. Tracheal reconstruction without the use of grafts. *Thorax* 1957; 12: 177-80.
4. GILBERT A, DESLAURIERS J, MCCLISH A, PIRAUX M. Tracheal sleeve pneumonectomy for carcinomas of the proximal left main bronchus. *Canadian Journal of Surgery* 1984; 27: 583-5.
5. SALZER GM, KROESSEN G, HOFER E. Catheter jet ventilation, a favourable technique during resection of the central tracheo-bronchial system. *Thoracic and Cardiovascular Surgeon* 1985; 33: 276-8.
6. CLARKSON WB, DAVIES JR. Anaesthesia for carinal resection. *Anaesthesia* 1978; 33: 815-9.
7. COPPEL DL, JOHNSTON JR. Ketamine infusions. *Anaesthesia* 1985; 40: 708.
8. ROGERS RC, GIBBONS J, COSGROVE J, COPPEL DL. High-frequency jet ventilation for tracheal surgery. *Anaesthesia* 1985; 40: 32-6.

The oesophageal detector device

Assessment of a new method to distinguish oesophageal from tracheal intubation

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Summary

A new method to distinguish oesophageal from tracheal intubation using the oesophageal detector device was evaluated. In 100 healthy adults, observers of differing experience reliably and rapidly detected 51 oesophageal and 49 tracheal intubations in a randomised, single-blind trial. In one case, blockage of the tracheal tube was detected swiftly and allowed corrective steps to be taken. This method can be used in patients with bronchospasm to detect correct tracheal placement when auscultation and decreased compliance of the chest may make clinical confirmation difficult. It can be concluded from this study that the oesophageal detector device is a reliable, rapid, inexpensive and easy to use method for the detection of oesophageal intubation and its very low cost should make it readily available in all situations where tracheal intubation is carried out.

Key words

Complications; oesophageal intubation.

Equipment; oesophageal detector device.

The Report on confidential enquiries into maternal deaths in England and Wales in 1979-1981¹ which was the subject of a subsequent editorial² revealed that eight of a total of 22 deaths attributable to anaesthesia were directly related to difficulty in tracheal intubation. In four patients the tube was definitely placed in the oesophagus but this was not recognised, with dire consequences.

Indeed, difficulties with tracheal intubation and the detection of oesophageal placement of the tube are recurring problems encountered by anaesthetists.²⁻⁹ Faulty tracheal intubation technique was deemed to be the cause of death or cerebral damage in 30.7% of anaesthetic accidents reported to the Medical Defence Union of the United Kingdom during the 8 years from 1970 to 1977.¹⁰ Thirty-seven deaths and 13 cases of cerebral damage resulted from inadvertent misplacement of the tube in the oesophagus.

A number of tests and observations have been suggested for the diagnosis of oesophageal intubation but the only one found to be totally reliable is the absence of carbon dioxide in the exhaled gas.^{3,11} This, however, requires the presence of carbon dioxide analysers in operating theatres, intensive care, accident and emergency and resuscitation units, and the cost is clearly prohibitive. Most anaesthetists rely on a high index of suspicion and clinical observation to diagnose oesophageal intubation. In the patient where hypoxia occurs after intubation, many adhere to the adage 'when in doubt, take it out',¹⁰ but this can cause its own problems if a correctly placed tube is removed when hypoxia is due to other causes. Clearly there is still a need for an

effective, simple and rapid method to detect oesophageal intubation or confirm tracheal intubation.

Methods

The oesophagus is a fibromuscular tube 25 cm long in adults that extends from the cricopharyngeal sphincter to the cardia of the stomach. There is no intrinsic structure to maintain its patency. The trachea extends from the cricoid cartilage to its termination at the tracheal bifurcation and in the adult it is about 10-12 cm long. Its diameter is related to the size of the subject and can vary from 13-22 mm. The trachea remains constantly patent due to C-shaped cartilages joined vertically by fibro-elastic tissue and closed posteriorly by unstriped trachealis muscle.

Apparatus and technique

The method is simple and takes seconds to perform; it utilises inexpensive equipment that is already available. The device consists of a 60-ml Plastipak catheter-tip syringe fitted to one end of a standard catheter mount with an International 15-mm tracheal tube fitting at the distal end. This I have termed the oesophageal detector device (Figs 1 and 2). The device must be airtight in order to function properly and this can be tested simply by occluding the distal end with a thumb and pulling back on the plunger. If resistance or negative pressure is felt it is suitable for use.

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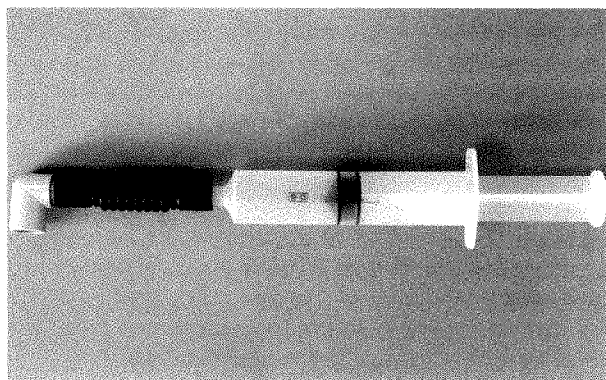


Fig. 1. The oesophageal detector device.



Fig. 2. The oesophageal detector device in use.

If the tracheal tube is correctly placed in the trachea and the oesophageal detector device is attached to it and an airtight seal ensured, withdrawal of the plunger of the syringe will aspirate gas from the patient's lungs without any resistance apart from that inherent in the device. However, if the tracheal tube is in the non-rigid oesophagus, withdrawal of the plunger of the syringe will cause apposition of the walls of the oesophagus around the tube, which will occlude the lumen and cause a negative pressure or resistance when the plunger is pulled back. This immediately alerts the clinician that the tracheal tube is incorrectly placed and allows appropriate steps to be taken.

Subjects

Healthy patients (ASA grades 1 and 2) aged between 16 and 80 years undergoing elective surgery where tracheal intubation, muscle relaxation and controlled ventilation were required as part of the anaesthetic technique were studied. Patients with oropharyngeal, tracheal, oesophageal or gastric disease were not included. Informed consent was obtained from all patients, as was local ethical committee approval.

Premedication was optional according to the anaesthetists' normal practice. Intravenous induction of anaesthesia was followed by administration of a muscle relaxant and intubation of the trachea in the normal manner. Controlled ventilation was established with 66% nitrous oxide and optional volatile anaesthetic agent in oxygen. When stable maintenance anaesthesia was established, as indicated by

clinical signs and monitoring of arterial blood pressure, heart rate and ECG, the oesophagus was intubated under direct vision, minimising the risk of trauma, and the oesophageal tube cuff was then inflated with 3–5 ml of air.

The patient's lungs were ventilated with 100% oxygen via the tracheal tube with an increased concentration of volatile anaesthetic agent to ensure continued adequate anaesthesia. After 5 minutes, the oesophageal tube was inflated with two tidal volume compressions of the reservoir bag of the breathing circuit with 100% oxygen to simulate normal procedure after intubation. The breathing system was then disconnected from both tubes.

A second observer, who had not witnessed the anaesthesia, was called in to assess the placement of one of the two tubes and decide whether it was in the trachea or oesophagus using only the oesophageal detector device and the technique outlined above.

Results

One hundred patients took part in the study, 30 males and 70 females with a mean age of 38.3 years. The anaesthetist observers included 11 consultants, three senior registrars, 11 registrars and six senior house officers. In addition, three surgeons, five anaesthetic nurses and an RAF paramedic took part as observers. Makes of Portex, Clearway, RAE, Polar, Vygon, Brandt and Armour latex tracheal tubes were used and their sizes ranged from 7.5 to 9.5 mm internal diameter.

There were 99 first-time correct identifications of tube placement, 51 oesophageal and 48 tracheal. The mean time taken by the observers to diagnose the tube placement correctly was 6.9 seconds, with a range of 5–16 seconds.

On only one occasion was the anaesthetist observer unsure of the placement of a tube in the trachea; that is, he initially aspirated gas without resistance but then obtained some resistance followed again by loss of resistance. In this patient, prior to the test, right bronchial intubation occurred initially and the tube was repositioned in the trachea. The airway pressure remained elevated at 3.0–3.5 kPa but the chest was clear on auscultation. When the test was carried out it gave an inconclusive result as described above. The tracheal tube was replaced and it was found to be almost totally blocked by thick purulent secretions. When the test was repeated on the same patient, it indicated unequivocally correct placement. The whole episode from detection of a possible obstruction of the tracheal tube to its change, took less than 90 seconds.

High airway pressure was noticed in another patient after the test had been carried out correctly. Right bronchial intubation was diagnosed by auscultation of the chest and some resistance was felt when the oesophageal detector device was used with the tube in this position. This resistance and the airway pressure decreased after the tip of the tube was withdrawn into the trachea.

There were two cases of moderate bronchospasm after intubation where the maximum airway pressures were between 3.0 and 4.2 kPa and rhonchi were heard. Tracheal intubation was correctly diagnosed in both these patients without any ambiguity.

Finally, one of the patients had an unsuspected difficult intubation due to limited mouth opening and full prominent dentition. Only the tip of the epiglottis could be seen on laryngoscopy and blind intubation of the trachea was

achieved with the aid of an introducer. The oesophageal detector device indicated that the tube was in the trachea and this was confirmed subsequently by clinical signs and capnography.

Nearly all of the observers found the device to be easy to use. No significant postoperative sequelae occurred as a result of this study.

Discussion

The cost of the oesophageal detector device is a fraction of that of the cheapest carbon dioxide analyser;¹² it does not require a power source or warm-up time and is maintenance-free and portable, which makes it suitable for field use. One potential cause of failure or delay in the detection of oesophageal intubation when carbon dioxide analysers are used, is when a patient has been given prophylactic magnesium trisilicate or sodium bicarbonate to neutralise gastric acid prior to induction of anaesthesia. Both drugs have been shown to produce carbon dioxide in their reaction with gastric acid and, in particular, 20 ml molar sodium bicarbonate can produce as much as 500 ml carbon dioxide gas,¹³ but this problem has not yet been reported.

It should be noted that this study did not include patients with oesophageal or tracheal disease, where distortion or alteration of normal anatomy may occur. It cannot be over-emphasised that the oesophageal detector device must always be checked for airtightness prior to use and the fittings between the catheter mount, syringe and tracheal connector must be airtight.

As a confirmatory test, the oesophageal detector device can also be used to inject a bolus of air into the tube while the anaesthetist listens over the epigastrium for gas bubbling in the stomach.³ This confirmatory test was not found to be necessary in the study to detect oesophageal intubation.

It can be concluded that this device is a reliable, rapid,

inexpensive and easy to use method for the detection of oesophageal intubation and its very low cost should make it readily available in all situations where tracheal intubation is carried out.

Acknowledgments

I thank all my colleagues who participated in the study and Drs I.S. Grant and I.G. Gray for their invaluable advice and support.

References

1. *Report on confidential enquiries into maternal deaths in England and Wales in 1979-81*. London: HMSO, 1986.
2. MORGAN M. The confidential enquiry into maternal deaths. *Anaesthesia* 1986; **41**: 689-91.
3. POLLARD BJ, JUNIUS F. Accidental intubation of the oesophagus. *Anaesthesia and Intensive Care* 1980; **8**: 183-6.
4. HOWELLS TH, REITHMULLER RJ. Signs of endotracheal intubation. *Anaesthesia* 1980; **35**: 984-6.
5. OGDEN PN. Endotracheal tube misplacement. *Anaesthesia and Intensive Care* 1983; **11**: 273-4.
6. PETERSON AW, JACKER LM. Death following inadvertent oesophageal intubation: a case report. *Anesthesia and Analgesia* 1973; **52**: 398-401.
7. CUNDY J. Accidental intubation of oesophagus. *Anaesthesia and Intensive Care* 1981; **9**: 76.
8. STIRT JA. Endotracheal tube misplacement. *Anaesthesia and Intensive Care* 1982; **10**: 274-6.
9. BATRA AK, COHN MA. Uneventful prolonged misdiagnosis of esophageal intubation. *Critical Care Medicine* 1983; **11**: 763-4.
10. UTTING JE, GRAY TC, SHELLEY FC. Human misadventure in anaesthesia. *Canadian Anaesthetists' Society Journal* 1979; **26**: 472-8.
11. BIRMINGHAM PK, CHENEY FW, WARD RJ. Esophageal intubation: a review of detection techniques. *Anesthesia and Analgesia* 1986; **65**: 886-91.
12. *Apnea monitors: product comparison system*. Maidenhead: McGraw-Hill, 1985; **12-575**: 1-13.
13. MACDONALD AG. *The gastric acid problem. Recent advances in anaesthesia and analgesia, No. 15*. Edinburgh: Churchill Livingstone, 1985.

An evaluation of the Stihler 1FT 200 blood warmer

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Summary

The performance of the Stihler 1FT 200 blood warmer was evaluated at flow rates from 25 to 150 ml/minute and compared with that of the Hetotherm and Fenwal warmers. The Fenwal proved to be an efficient apparatus at all flow rates but the performance of the Hetotherm fell off slightly at higher flow rates. The Stihler 1FT 200 did not meet requirements for use in the operating room.

Key words

Equipment; blood warmers.

The need for warming blood prior to transfusion, particularly when the latter is massive, is firmly established. The two basic methods of achieving this are either to warm the blood before infusion or to do it during infusion. We report here an investigation of a new blood warmer of the latter type, the Stihler 1FT 200.



Fig. 1. Stihler 1FT 200 blood warmer.

Methods

Description

The Stihler 1FT 200 blood warmer is shown in Fig. 1. The heating unit consists of an aluminium cylinder which is grooved in order to accommodate the blood warming coil (Fig. 2), and can accommodate up to six windings (240 cm in length, 4 mm external diameter). A metal sleeve is provided which fits over the heating element and ensures maximum heat conduction and minimises heat loss. This is shown in place in Fig. 1.

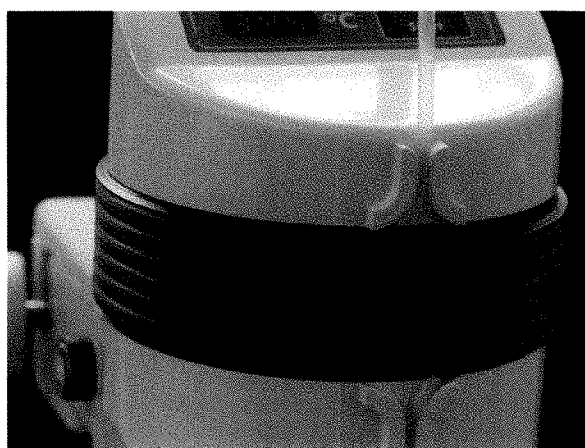


Fig. 2. The warmer showing the grooved aluminium heating cylinder.

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The temperature, measured in the aluminium unit, is fixed and shown on the top of the apparatus; this has a safety cutoff set at 41°C when the machine automatically switches itself off. This is accompanied by an audible and visual alarm. The apparatus has a warm-up time of 90 seconds.

The performance of this blood warmer was compared with two others that are in use in this hospital, namely, the Hetotherm (Heto, 3460 Birkerød, Denmark) which is an agitated water bath warmer, and the Fenwal (Travenol Ltd, Compton, Berkshire) which is a dry warmer that uses a thin polythene bag between two heating plates.

Procedure

An infusion set was connected to the blood warming coil (bag in the case of the Fenwal), which was arranged so that 40 cm emerged from the warmer. This was inserted into a thermistor thermometer which was sealed into one arm of the Y-piece so that the temperature of the issuing fluid was measured continuously. A similar arrangement was used to measure the input temperature just before the warming element.

The fluid used was saline, bags of which had been kept in a refrigerator. The starting temperature of the saline was between 6 and 8°C prior to each set of measurements. The output temperatures were measured at flow rates of 25, 50, 75, 100, 125 and 150 ml/minute. Both three and six coils were used with the Stihler warmer. The experiments were repeated on three occasions for each warmer.

Results

The results are shown in Fig. 3; there was virtually no variation within each test. The output temperature was maintained above 32°C at all flow rates by the Fenwal warmer. The output temperature decreased below 32°C at flow rates greater than 75 ml/minute and barely reached 28°C at 150 ml/minute with the Hetotherm. The output temperature was well below 32°C at all flow rates using three coils with the Stihler 1FT 200 and decreased progressively as the flow increased. When six coils were used, a temperature above 32°C was achieved at 25 ml/minute but thereafter the temperature decreased markedly with increasing flow rates and reached only 14°C at 150 ml/minute.

Discussion

The specifications for blood warming apparatus were discussed by Russell.¹ The apparatus must be easy to use and maintain, must warm blood rapidly and preferably be unobtrusive. It must be capable of providing blood at a temperature above 32°C at flow rates up to 150 ml/minute. One unit of blood would be delivered at this flow rate in about 3 minutes, which is about as fast as is practicable. The heating device must not damage the blood.

The Stihler 1FT 200 is a light, neat unit, very easy to set up and operate and is readily attached to an infusion stand. Similar remarks apply to the Fenwal but the Hetotherm is more cumbersome and more difficult to set up. The performance of the Stihler 1FT 200 fell well below that required. Russell¹ has calculated that the minimum heating power required to ensure that blood at 4°C is warmed to 32°C or

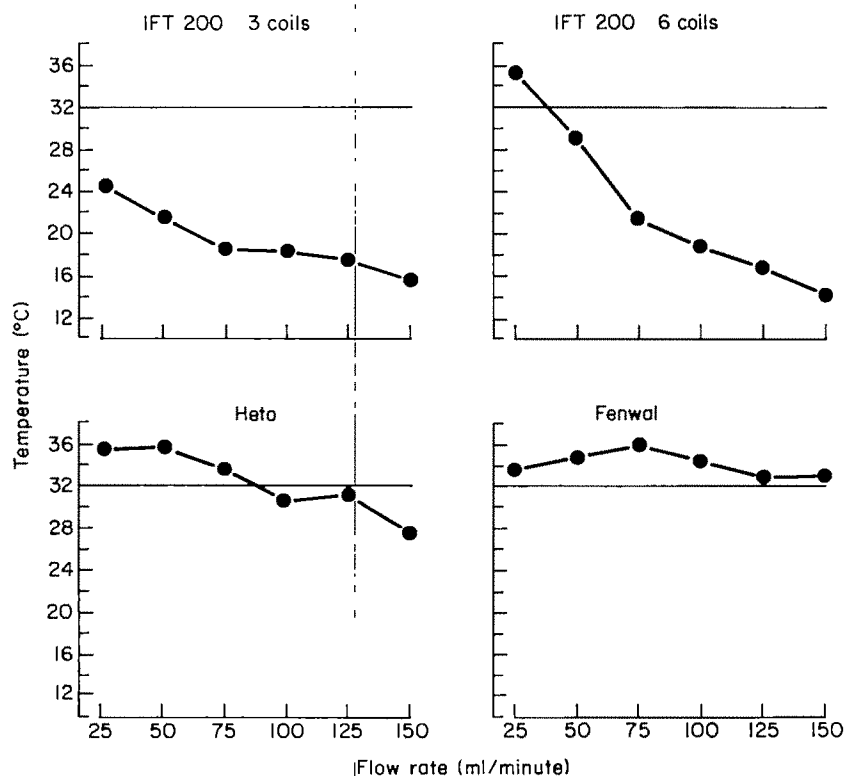


Fig. 3. Output temperature of the Stihler IFT 200 blood warmer using three and six coils and of the Hetotherm and Fenwal warmers at flow rates from 25 to 150 ml/minute.

above at a flow rate of 150 ml/minute is 310 watts. The output of the new warmer is only 75 watts, so it is not surprising that it did not meet the necessary requirements. The Fenwal (output 700 watts) achieved the requirements and even the Hetotherm, with an output of 610 watts, was unable to maintain an outflow temperature above 32°C at the higher flow rates.

The Stihler IFT 200 blood warmer is advertised as easy to handle and with a high performance, especially for massive transfusion. We agree with the former claim but the latter one has not been validated by this investigation and it is concluded that, in its present form, this unit is not suitable for use in an operating room environment.

Acknowledgments

We would like to thank Mr C. Bolter of Camino for the loan of the blood warmer and Mrs S. Richens for secretarial assistance.

Reference

1. RUSSELL WJ. A review of blood warmers for massive transfusion. *Anaesthesia and Intensive Care* 1974; **2**: 109–30.

Pressure infusor devices

Do they generate the pressures indicated?

P. COX

Summary

Three currently available pressure infusor devices, based on three different principles, were tested to see if the pressure reading on the infusor manometer corresponds to the pressure generated in the infusion system. Each device was tested in two ways. First, the pressure generated in the infusion system was measured when the infusor bag pressure was maintained at 300 mmHg while the infusion bag was emptied in aliquots of 50 ml. Second, the pressures in the infusor bag required to maintain a pressure of 300 mmHg were measured as the infusion bag was emptied stepwise.

The results reveal surprisingly large discrepancies between the pressure registered on the infusor manometer and the actual pressure generated in the fluid, which are not due to manometer inaccuracy. The degree of discrepancy depends on the amount of fluid that remains in the infusion bag and, when the infusor manometer shows a pressure of 300 mmHg, pressure in the fluid can be as much as 170 mmHg above or 200 mmHg below this value. Furthermore, it was impossible to maintain a pressure of 300 mmHg in the infusion system using one of the devices despite the fact that 100 ml fluid remained. The clinical significance of these findings is discussed.

Key words

Apparatus; pressure infusor device.

Monitoring; arterial pressure.

The use of pressure infusor devices is widespread in the field of anaesthesia and intensive care. Their use may be indicated whenever resistance to flow in an infusion system prevents attainment of the infusion rate required. Such resistance may result from the use of small gauge cannulae or long catheters, of highly viscous fluids such as erythrocyte concentrate, or simply because the flow rate requirement is excessively high. They are also used in invasive arterial pressure monitoring where they generate the driving pressure for constant flush devices.

The most common design of pressure infusion devices today consists of a pneumatically filled infusor bag that lies together with the infusion bag in a confined situation. The pressure in the infusor bag is thus transferred to the fluid that is infused. All infusor devices are provided with a manometer that registers the pneumatic pressure in the infusor bag. It would seem logical to assume that this pressure represents that in the infusion system but whether this is so, has not been investigated previously.

Three currently available infusor devices were tested to see if the pressures generated in the fluid in the infusion bag corresponded to those registered on the infusor device manometer.

Materials and methods

The infusors

Three different types were considered in this study. The first type is a non-distensible pressure bag that has sewn onto its side a nylon net open at both ends so as to allow insertion of the infusion bag between the net and the pressure bag. The pressure created when the infusor bag is inflated, compresses the infusion bag against the net and thus generates pressure in the fluid system. This is commonly known as the Fenwal infusor and the version tested is produced by Pharma and named the Biotest (Fig. 1).

The second type consists of a pressure bag that more or less embraces the infusion bag. The pressure generated when the infusor bag is inflated, is applied evenly around the infusion bag. The version tested is produced by Medex Inc. and named the C-Fusor. It is made of strong clear plastic and is held in place by a Velcro band after this is wrapped around the infusion bag (Fig. 2).

The third type is based on the principle that the infusion bag is placed together with the infusor pressure bag inside a rigid box. When the infusor bag is inflated the infusion

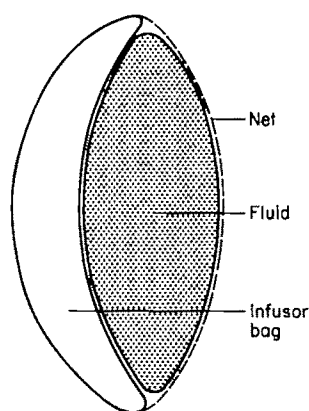


Fig. 1. Diagrammatic cross-section of the Biotest device.

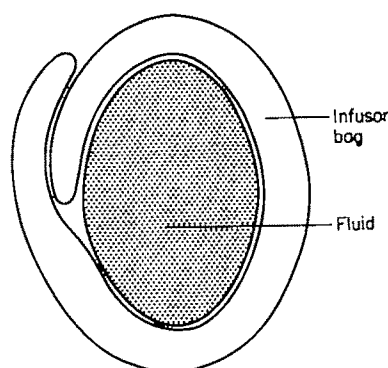


Fig. 2. Diagrammatic cross-section of the C-Fusor device.

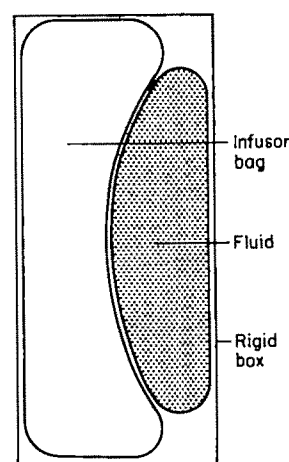


Fig. 3. Diagrammatic cross-section of the Lamtec device.

bag is compressed against the front side of the box which is a clear perspex window. This type is commonly known as the Norfolk and Norwich infusion box¹ and the version tested is manufactured by the Lamtec Medical Equipment Company Ltd (Fig. 3).

Pressure measurements

Pressure measurements were made with a Hewlett-Packard quartz transducer type 1290A coupled to a Hewlett-Packard 78342A amplifier. The giving set from the infusion bag was connected via a three-way tap to the dome of the pressure transducer. The transducer was always held at the same level in relation to the infusion bag, i.e. at the lower border of the bag. For each run of pressure readings a new infusion bag (Travenol) that contained 500 ml 5% glucose solution was used.

Infusor manometer check. A direct line was set up between the infusor pressure bag and the transducer so as to be able to compare pressures registered by the infusor device manometer and those registered by the pressure transducer. The infusor bag was inflated to various pressures between 0 and 400 mmHg. The pressures registered by the infusor manometer and the transducer were compared.

Measurements. The first series of measurements was conducted in order to determine the efficiency of the infusor device in maintaining pressure in the infusion system as the volume of fluid that remains becomes less. A bag of 500 ml 5% glucose was placed in the infusor device and the infusor device inflated until a pressure of 300 mmHg was measured by the transducer. The pressure registered on the infusor manometer was noted and 50 ml fluid released from the infusion bag. The infusor bag was then further inflated until the pressure measured by the transducer was once again 300 mmHg. The new reading on the infusor manometer was noted and the whole procedure repeated. This was carried out until no fluid remained or until the pressure required to maintain 300 mmHg could not be attained by the infusor device.

A second series of measurements was conducted to determine the actual pressures generated in the infusion system when the infusor device is inflated until the manometer reads 300 mmHg. A 500 ml bag of 5% glucose solu-

tion was placed in the infusor device and the infusor bag inflated until the manometer read 300 mmHg. The actual pressure generated in the fluid system was then measured on the transducer. Fifty millilitres of fluid were then released from the bag and the infusor further inflated to give a pressure of 300 mmHg on the manometer. The pressure measured by the transducer was once again noted and the whole procedure repeated. This was done until no fluid remained in the bag or until the pressure in the fluid system decreased to that caused by the column of fluid that remained.

For each series and for each device, five infusion bags were emptied and pressure measurements made as described above. Every measurement was double-checked and the mean values and standard deviations calculated.

Results

The readings given by the manometers, taking into account their rather sparsely marked, large scaled facings, agreed satisfactorily with those given by the transducer. The results of the first measurement series are depicted in Table 1 and in graphical form in Fig. 4. It can be seen that with the Biotest greater pressure was required to maintain a pressure of 300 mmHg in the infusion system and, once the volume in the infusion bag had decreased to 150 ml, the pressures required rapidly became impractical and the pressure in

Table 1. Pressure in the infusor bag required to maintain a pressure of 300 mmHg in the infusion system as the volume of fluid that remains becomes less. Values expressed as mean (SD).

Volume remaining, ml	Pressure, mmHg		
	Biotest	C-Fusor	Lamtec
500	277 (2.4)	168 (2.4)	170 (2.0)
450	290 (1.0)	180 (3.2)	189 (2.4)
400	305 (4.2)	190 (3.5)	209 (2.1)
350	335 (3.5)	199 (3.2)	225 (1.4)
300	373 (6.7)	204 (2.0)	238 (2.3)
250	420 (12.4)	214 (4.3)	252 (1.7)
200	485 (10.1)	234 (4.2)	263 (2.0)
150	555 (19.9)	283 (4.0)	273 (1.8)
100	> 700	361 (12.0)	281 (1.7)
50	—	> 700	292 (1.6)
25	—	—	303 (2.6)

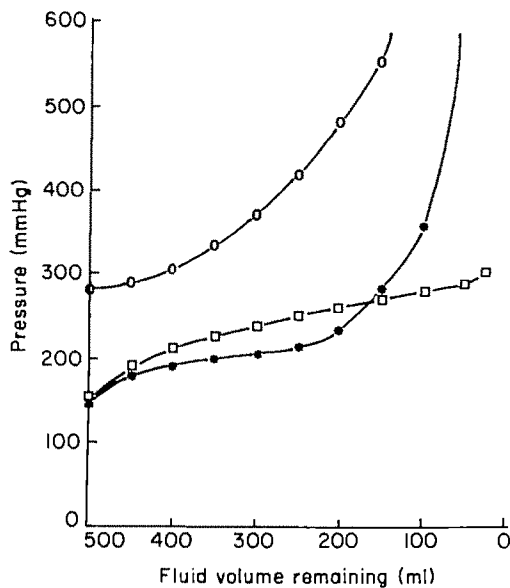


Fig. 4. Pressure in the infusor bag required to maintain a pressure of 300 mmHg in the infusion system as the volume of fluid that remains becomes less. O, Biotest; *, C-Fusor; □, Lamtec.

the fluid system rapidly decreased to that caused by the column of fluid that remained. The C-Fusor also required inflation to high pressures once the volume of fluid that remained had decreased to 100 ml if a pressure of 300 mmHg was to be maintained, whereas the Lamtec device was able to maintain this pressure without the need for high infusor bag pressures even when only 25 ml fluid remained.

Table 2. Pressure generated in the infusion system when the pressure reading on the infusor manometer is maintained at 300 mmHg as the volume of fluid that remains becomes less. Values expressed as mean (SD).

Volume remaining, ml	Pressure, mmHg		
	Biotest	C-Fusor	Lamtec
500	325 (2.2)	445 (2.1)	472 (5.9)
450	311 (3.6)	429 (3.6)	431 (2.6)
400	293 (4.4)	417 (2.5)	402 (2.9)
350	273 (7.7)	409 (2.8)	378 (2.9)
300	238 (9.4)	400 (3.7)	361 (1.9)
250	202 (2.8)	389 (3.4)	346 (2.7)
200	173 (4.3)	360 (6.1)	334 (1.8)
150	145 (3.2)	308 (6.0)	324 (1.5)
100	114 (7.0)	238 (6.1)	315 (2.3)
50	54 (3.2)	87 (14.5)	303 (2.6)
25	22 (3.8)	14 (2.3)	281 (5.8)

The results of the second series are presented in Table 2 and Fig. 5. It can be seen that there is little correlation between the pressure generated in the infusion system and that registered on the infusor device manometer. In the case of the Lamtec and C-Fusor devices, the fluid pressure generated with full infusion bags could be as high as 470 mmHg when the device manometer read 300 mmHg or, in the case of the Biotest, as low as the pressure caused by the column of fluid that remained even when 100 ml fluid was left.

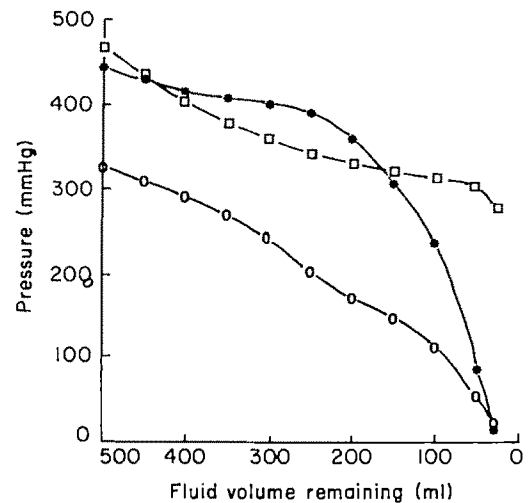


Fig. 5. Pressure generated in the infusion system when the pressure reading on the infusor manometer is maintained at 300 mmHg as the volume of fluid that remains becomes less. O, Biotest; *, C-Fusor; □, Lamtec.

Discussion

The results presented here demonstrate that there may be large discrepancies between the pressure registered on the infusor device manometer and that actually generated in the fluid that is infused. It would seem logical to assume that two inflated or filled non-distensible bags pressed together should have the same pressures within their walls. In practice this may not be the case, due to a complex combination of factors which includes the differing areas and curvatures of contact between the two bags and between the bags and the structures that surround them.

Reliability and precision are two essential features of medical equipment. It is surprising, therefore, that infusor pressure devices have not been checked to determine the actual pressures they generate. The important question, however, concerns the clinical significance of these results.

Infusor pressure devices have been used in many departments over a great many years yet, to the author's knowledge, the literature contains no reports of mishaps that have resulted from their use. As mentioned previously, they are used in three basic situations: firstly, to overcome resistance to flow caused by the infusion of viscous fluids such as blood, especially if these are infused through small cannulae or long catheters or blood warmers; secondly, to increase infusion rates whenever these are inadequate in view of the clinical situation, for example in the case of shocked or hypovolaemic patients; and thirdly, as the driving pressure for constant flow devices in invasive arterial pressure monitoring. It may also be mentioned that they are employed in some centres for the infusion of cardioplegic solutions through the coronary circulation under pressure.

In the first two situations the endpoint which is desired is the attainment of an infusion rate that meets the clinical requirement. Naturally, the pressures that exist in the infusion system in no way represent the pressure situation in the vessel in which the cannula lies. A large pressure gradient exists over the cannula as long as there is free flow in the vessel. Should, however, the vessel become occluded distal to the tip of the cannula then pressure in the vessel will increase towards that in the infusion system. This also applies if the cannula tip comes to lie outside the vessel, in

which case high pressures may build up in the tissues. The author has previously measured the pressure in the vein distal to the cannula tip prior to and during rapid infusion of fluid at 300 mmHg. The change in pressure was negligible.

In these situations it is a prerequisite that infusor devices should be employed only as long as it can be said with certainty that the cannula/catheter lies well within a sizeable vein or artery. If this prerequisite is observed then the discrepancies described between the infusor manometer and the actual pressure in the infusion system have no practical significance.

The makers of the constant flow devices stipulate a precise hydrostatic pressure that is required to achieve a given flow rate when they are used in invasive pressure monitoring. Should the pressure be higher then, naturally, the flow will also be higher but it is unlikely that this will have any clinical significance with the low flow rates involved. If, however, the pressure is too low then the flow rate may decrease to levels where clotting within the cannula/catheter occurs.

Direct measurement of the pressure in the fluid system connected to the constant flow device can easily be made using the pressure transducer with the flush device fully open and the tap to the cannula closed. The infusor device can then be inflated or deflated until the correct driving

pressure is obtained. If a note of the pressure registered on the infusor manometer is made and this pressure reading maintained throughout the day, then this need only be checked two or three times daily especially if one of the efficient devices such as the C-Fusor or Lamtec is used and a new 500 ml infusion bag is replaced daily.

The Lamtec device seems to be the most suitable in terms of effectiveness in emptying infusion bags rapidly, since the pressure required to maintain a fluid pressure of 300 mmHg remains at or below 300 mmHg until the very last few millilitres remain. In emergency situations, where valuable blood is forced rapidly through a warmer, it is highly irritating to have blood remaining when pressure in the bag decreases. This applies especially to the Biotest device.

In conclusion, the discrepancies that can exist between the pressure registered on the infusor manometer and the actual pressure generated in the infusion system, probably have no practical significance as long as meticulous technique and observation are employed. It is important, however, to be aware that such discrepancies exist.

Reference

1. CHAPMAN RB, KEEP P. The Norfolk and Norwich infusion box. *Anaesthesia* 1980; 35: 1211-4.

A combined oxygen concentrator and compressed air unit

Assessment of a prototype and discussion of its potential applications

W. R. EASY, G. A. DOUGLAS AND A. J. MERRIFIELD

Summary

A prototype combined oxygen concentrator and air compressor is described. Laboratory assessment demonstrated satisfactory oxygen concentrations, flows, pressures and reliability. Its various modes of use in clinical practice are described. It is likely to be a valuable method to provide oxygen for anaesthesia both in remote areas and where nitrous oxide-free anaesthesia is required, as well as a reliable alternative to commercially produced oxygen for therapeutic purposes.

Key words

Equipment; oxygen concentrator.

Interest in medical oxygen concentrators continues to expand rapidly in response to their increased acceptance as alternative sources of oxygen.¹ They offer economic and logistic advantages over conventional compressed or liquid supplies.² The compact size and portability of domiciliary concentrators are arousing particular interest amongst anaesthetists both in the UK^{2,3} and in developing countries.⁴ The apparatus evaluated in this paper and recently described,⁵ was developed to expand the application of the small oxygen concentrator into routine anaesthesia and ventilation.

The basis of the unit tested* is a two-column pressure swing adsorber (PSA) oxygen concentrator which employs artificial zeolite to adsorb atmospheric nitrogen. Two electrically powered compressors (240 volt, 50 cycle, 300 watt) are housed in the base of the unit (Fig. 1). The first compressor supplies air at 140 kPa to the concentrator. Pressure switching between columns is performed pneumatically at approximately 20-second intervals, and the oxygen-rich product is fed via a 0–5 litres/minute flowmeter and two-way valve either to a low pressure outlet or to the intake of the second compressor. The latter supplies air or oxygen-enriched air to a Schrader high pressure outlet at approximately 300 kPa. Air entrained by the compressors passes through 0.3- μ m bacterial filters (Pall). A Bourdon-type pressure gauge is incorporated in the high pressure outlet line. The unit may be used in a number of ways.

* Manufactured by Pneupac (Kay Pneumatics) Ltd, 45 Crescent Rd, Luton, Beds.

Low flow, high oxygen concentration (Fig. 2a). Gas with an oxygen concentration of approximately 95% (v/v) flows at 2–3 litres/minute. This gas may be used to supply a mask for oxygen therapy or to enrich entrained air in a drawover system such as the Triservice anaesthetic apparatus.⁶

Low flow, high oxygen concentration gas and compressed air separately (Fig. 2b). Compressor 1 and the concentrator supply high oxygen concentration gas to the anaesthetic system. This gas can be drawn through a suitable vaporizer by a ventilator which is powered by the high pressure air from compressor 2.

Compressed air–oxygen mixture (Fig. 2c). Compressor 1 drives the concentrator and the gas product is fed to compressor 2. The oxygen-enriched compressed air thus obtained operates a compact ventilator driven by respirable gas, such as the PneuPac,* or the pressure may be reduced by a suitable regulator and the gas then used to operate a minute volume divider type of ventilator. In either situation the ventilator may be used for intermittent positive pressure ventilation and may be connected to a suitable vaporizer for anaesthesia.

Methods

The unit was set up in the laboratory and its performance evaluated solely as an oxygen concentrator, solely as an air compressor or as a combined oxygen concentrator and air compressor.

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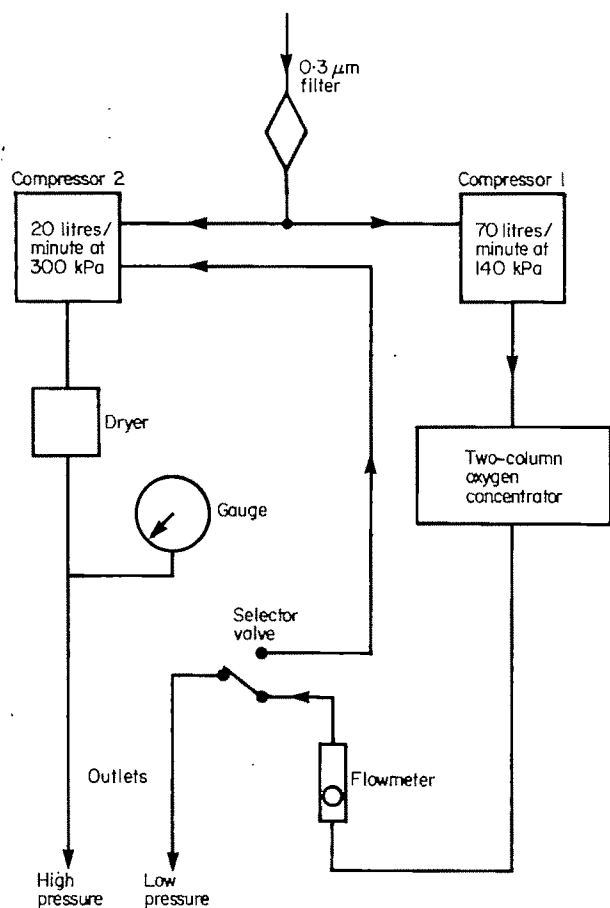


Fig. 1. Internal diagram of concentrator illustrating basic components. The switches, flow meter, pressure gauge and high-pressure outlet are grouped together on a control panel.

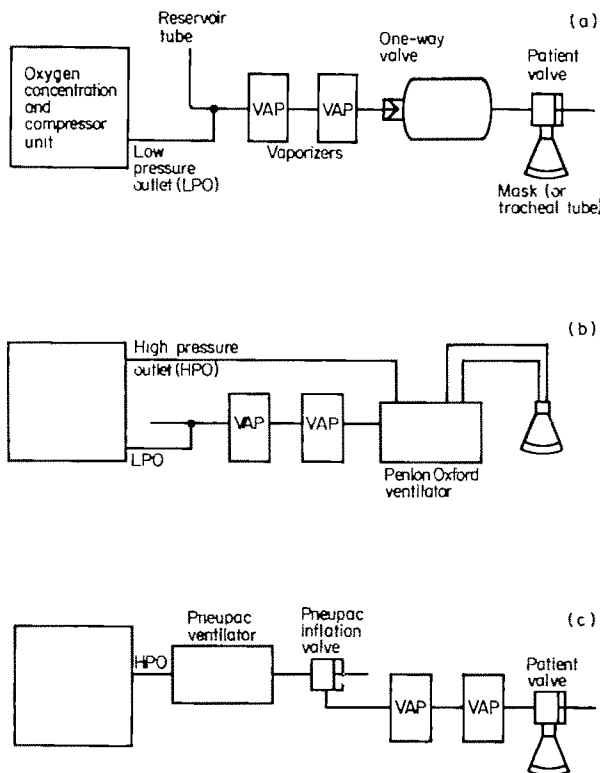


Fig. 2. Diagram illustrating modes of use as described in the text.

Oxygen concentrator alone

The following were measured: maximum oxygen concentration achieved; maximum oxygen concentrations at various concentrator flows; time from switch-on to reach maximum oxygen concentration, and time to 90% of maximum, both when the unit was cold (after it was switched off for a period exceeding 12 hours) and when warm; cyclical variation in oxygen concentration (both magnitude and frequency); maximum pressure of oxygen generated; and the effect on outflow of the addition of a Lifecare Duomask† and a Vickers Ventimask.‡

Air compressor alone

The following were measured: the maximum pressure generated by the compressor and the maximum flow produced.

Oxygen concentrator combined with compressor

This produced oxygen-enriched air at approximately 300 kPa. The following were measured: the variation in oxygen concentration with changes in concentrator flows, and the variation in oxygen concentration when used to drive a Pneuapac ventilator at various minute volume settings.

Laboratory measurements were performed and recorded by two of the authors. They were made at ambient temperature (20°C) and pressure (101.4–102.0 kPa). Oxygen concentrations were measured on 10 occasions for each variable, and the low flows from the concentrator were measured over 10 periods of one minute each. Five readings of the high flows were taken with the dry gas meter, each over a period of 10 minutes. Both the low pressure from the oxygen concentrator and the high pressure from the air compressor were also measured five times. Flows through the oxygen masks were measured with the facepiece modified so that a leak-free connexion could be made directly to the central boss. To ascertain the oxygen concentrations delivered by the two masks, gas was sampled from under the mask close to the external nares of a conscious, spontaneously breathing subject whose tidal volume was approximately 500 ml and respiratory rate 12 breaths/minute.

Oxygen concentrations throughout the assessment were measured using a paramagnetic oxygen analyser accurate to 1% oxygen (Sybron Taylor, Servomex OA 580A). This was calibrated and checked frequently with ambient air and 100% oxygen. It was coupled to a twin-channel recorder (Lectromed 216) through an amplifier (Lectromed MX2P762). The low flows examined in the first group were measured using a rolling seal spirometer (Morgan Spiroseal); this is stated by the manufacturers to have an accuracy of ±0.025 litres over the range 0–8 litres, and this was confirmed by a one-litre calibration syringe. Oxygen concentrator product pressures were measured with a transducer (Gould) calibrated against a mercury column. The second group of investigations involved the measurement of much higher pressures and flows. This was achieved

† Lifecare Duomask, Lifecare Hospital Supplies Ltd, 28A Scotland Rd, Market Harborough, Leics. LE16 8AX.
 ‡ Vickers Ventimask, Vickers Medical, Priestley Rd, Basingstoke, Hants. RG24 2NP.

Table 1. Flow indicated by concentrator flowmeter compared with flows measured with spirometer.

Indicated flow, litres/minute	Measured flow, litres/minute	Mean (SD), litres/minute	Predicted mean actual flow, litres/minute	95% range for possible actual flows, litres/minute
5	5.3 5.4 4.9 5.0 4.7 4.9 4.8 4.7	4.96 (0.26)	4.93	4.32–5.55
4	4.4 4.2 3.9 3.8 3.8 3.9 3.8 3.8	3.95 (0.23)	3.98	3.44–4.53
3	3.2 3.4 2.8 2.9 3.1 3.0 3.1 2.9	3.05 (0.19)	3.04	2.59–3.49
2	2.2 2.1 2.1 2.1 2.0 2.0 2.1 2.0	2.08 (0.07)	2.09	1.93–2.26
1	1.1 1.1 1.2 1.1 1.2 1.2 1.1 1.2	1.15 (0.05)	1.15	1.03–1.26

using a Bourdon-type gauge calibrated against a certified Budenberg standard test gauge and with a dry gas meter and stopwatch. The dry gas meter (Singer DTM115) had an accuracy stated by the manufacturers to be $\pm 0.5\%$ at flows up to 50 litres/minute.

Results

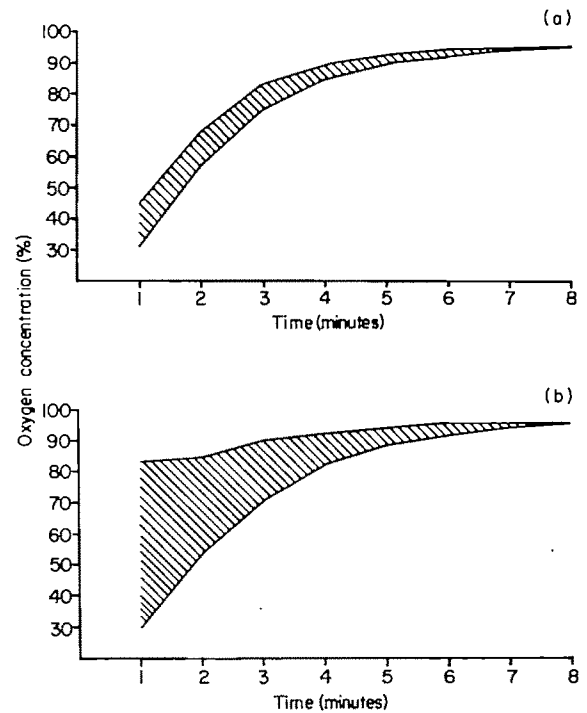
Some difficulty was experienced with the flowmeter on the oxygen concentrator prototype, in that the control was rather coarse and the bobbin tended to stick. (The flowmeter was inclined at 20° to the vertical but it worked more satisfactorily when removed and held vertically; this problem has been rectified on the later production prototype.) The degree of variation of indicated flow against flow measured with a rolling seal spirometer is shown in Table 1. The relationship between the indicated flow values and the measured flow values (which are known to be accurate to ± 0.25 litres) was assessed using weighted regression.⁷ The expected ranges of actual flow values associated with a given indicated flow value, derived from the regression, are also shown in Table 1. Concentrator flows quoted are therefore as obtained with the spirometer.

Oxygen concentrator alone

Figures 3a and b show oxygen concentrations against time for cold and warm starts, respectively, with the concentrator set to deliver 2 litres/minute. It can be seen that the maximum concentration achieved was invariably 95% and was always reached within 7 minutes. There was wide variation in the oxygen concentration delivered during the first 3 minutes but the mean time to 90% of maximum concentration (85.5% oxygen) was 3.62 minutes (SEM 0.0554, $n = 10$) for cold starts, and 3.48 minutes (SEM 0.2555, $n = 10$) for warm starts.

Figure 4 illustrates the inverse relationship between flow and oxygen concentration which is an inherent characteristic of PSA devices. When concentrator flows greater than 2 litres/minute were used, a cyclical variation of delivered oxygen concentration was noted at a frequency of 0.05 Hz which coincided with the switching frequency between columns (Table 2). The oxygen concentrations plotted in Fig. 4 are the mean values listed in Table 2.

The pressure of the product gas from the oxygen concentrator showed a small cyclical variation about a mean of 28.6 kPa (28.4–28.8 kPa). This pressure was achieved within seconds of switch-on. No difference in flows was detected due to the addition of a Lifecare Duomask or a Vickers Ventimask. The oxygen percentages measured from these masks are shown in Table 3.

**Fig. 3.** Relationship between oxygen concentration of concentrator product gas at 2 litres/minute, and time from switch-on. (a) Cold starts; (b) warm starts. The graph illustrates the range of concentrations measured at various times.**Table 2.** Cyclical variation in oxygen content of concentrator product gas at various flows.

Flow (litres/minute)	Mean oxygen concentration (% v/v) ($n = 5$)	Mean oxygen concentration variation (% v/v)	SEM
1	95.0	0	0
2	95.0	0	0
3	88.5	2.34	0.32
4	74.6	4.66	0.19
5	62.8	7.08	0.41

Air compressor alone

The air pressure at the Schrader outlet, measured at zero flow, was 307 kPa and the flow was constant at 38.7 litres/minute.

Oxygen concentrator combined with compressor

Gas was sampled with the concentrator set to deliver various flows. The results are presented in Fig. 5. It can be

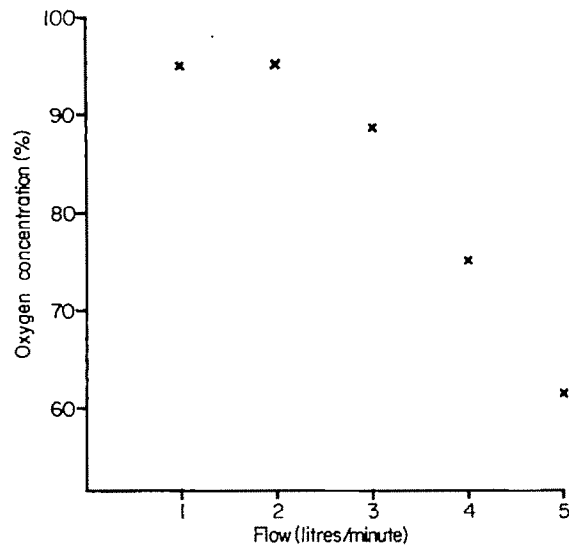


Fig. 4. Relationship between concentrator flow and oxygen concentration of product gas. Each plot is the mean of 10 measurements. Standard deviations were calculated but were too small to be represented.

seen that the oxygen concentration in the high pressure gas varied from 26% at 1 litre/minute to a maximum of about 33.5% at concentrator flows of 3–9.4 litres/minute. A flow within this range (4 litres/minute) was chosen to measure the oxygen concentrations achieved when the mixed gas outflow was used to drive the Pneupac ventilator (Table 4). The Pneupac settings were arbitrary and corresponded to approximately equidistant divisions of the range of settings provided by the volume/frequency control knob on the Pneupac. The tidal and minute volumes for each setting are shown, together with the variation in pressure measured in the supply line to the Pneupac.

Discussion

This study was undertaken to establish whether or not the prototype oxygen concentrator and ventilator power source, which is now 2 years old, could provide a useful supply of gas with an oxygen concentration that approached 100% and, in addition, a source of oxygen-enriched air at a pressure suitable to power a gas-driven ventilator. The methods used employed laboratory equip-

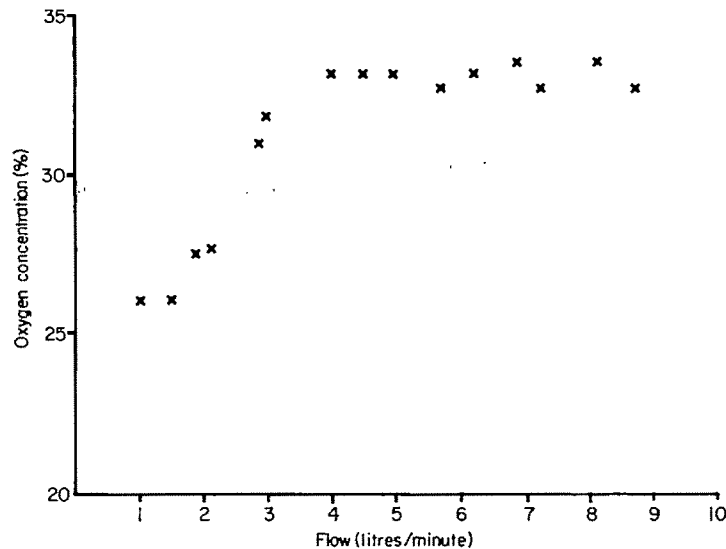


Fig. 5. Oxygen concentration of compressed air-oxygen mixture at various concentrator flows. Measurements taken on a single run.

Table 3. Predicted and measured oxygen concentrations with the 28% Ventimask (Vickers) and Duomask (Lifecare).

	Nominal output 100% oxygen, 4 litres/minute	Measured output 100% oxygen, 4 litres/minute	Calculated output concentrator product, 4 litres/minute	Measured output concentrator product, 4 litres/minute
Ventimask	28%	28%	26%	26%
Duomask	40%	44%	34%	35%

Table 4. Oxygen concentrations and other variables at various Pneupac settings.

	Setting						
	1	2	3	4	5	6	7
Tidal volume (litres)	0.15	0.19	0.22	0.35	0.46	0.82	1.17
Minute volume (litres)	4.1	4.5	4.85	5.9	6.4	9.03	11.5
Supply pressure during gas flow (kPa)	290	290	276	276	262	248	241
Oxygen concentration (% v/v)	35	36	36	36	36	36	36

ment which yielded an accuracy greater than that required for normal clinical purposes, and gave reproducible results.

At flows of 2 litres/minute the concentrator produced an oxygen concentration of 95%, which is an acceptable alternative to 100% oxygen⁸ and would, for example, be suitable for use with nasal oxygen specula. Most oxygen therapy masks in common use need a flow of 4 litres/minute, at which flow this unit produces 75% oxygen. It was established that the additional resistance to flow imposed by two commonly used masks does not adversely affect concentrator performance, but the percentage of oxygen delivered by such masks will be less than that specified by the manufacturers when used with 100% oxygen. The percentages which were measured (35% for the Duomask and 25.6% for the Ventimask) were close to those which we anticipated from calculation (34% and 26%) and the differences are quite acceptable for therapeutic purposes.

The small cyclical variation in oxygen percentage noted to occur at higher flows is an intrinsic feature of pressure swing adsorption. The different times taken to reach maximum oxygen concentration when the unit was started from warm and cold, appeared to be related to the stage in the cycle at which the concentrator was previously switched off. The smaller variation in time for the cold starts reflects the continuing equilibration and nitrogen adsorption after the unit is turned off.

The oxygen concentration of 36% measured when used with the Pneupac is a satisfactory level for most anaesthetic applications and is suitable for ventilated patients unless there is a major disturbance of gas exchange. The oxygen concentration in the gas delivered by the Pneupac was greater than when the Pneupac was not connected and there was minimal resistance to gas outflow. This probably relates to the cyclical reductions in flow through the second compressor that result from the ventilator cycling.

A supply of gas that contains about 33% oxygen at a pressure of 3 bar is easily adaptable for use with other ventilators, such as minute volume dividers, if the pressure is reduced. This was demonstrated by passing the gas through a variable pressure regulating valve (Norgren RO6) and using it to drive a Pulmovent MPP. It was found that the supply pressure was critical over a fairly small range and it is therefore recommended that a fixed pressure regulator is used for this type of ventilator.

The potential benefits of oxygen concentrators where compressed or liquid oxygen supply is expensive or logistically difficult, have been discussed extensively in the literature. Areas of application include developing countries,^{4,9} military and field situations,² major disasters,¹⁰ ambulances and aircraft.¹¹ This concentrator was developed with such applications in mind, and is adaptable to anaesthesia or therapeutic ventilation using a combination of the Triservice apparatus and Pneupac or Penlon Oxford ventilators. It could form the basis of a compact, self-contained anaesthetic machine for use in any hospital but particularly those in island, remote mainland and offshore locations (including ships), since it requires only mains electrical power to supply it. Furthermore, it offers a low cost method to supply a nitrous oxide-free anaesthetic carrier gas for applications in general anaesthesia where this is indicated. It is dependent on a 240 volt electricity supply but the power required (600 watts) is low and it could be powered by a portable generator if a mains source were not available. This extends its potential sphere of

application to ambulances or, indeed, any vehicle on which a generator can be mounted. At about 70 kg, the prototype tested is not easily portable but the weight of the production model will be reduced by use of lighter materials for the casing. It is also possible that it may be marketed as two modules for easier portability in field use. It is desirable that oxygen concentration is monitored periodically,¹¹ since the performance of the zeolite can deteriorate if it is exposed to hydrocarbons. (Some zeolites do not perform well when saturated with water vapour; this is not a problem with the particular zeolite used in this concentrator.) Advances in compressor technology have reduced servicing requirements to a frequency and nature that are within the capabilities of a reasonably practical anaesthetist, and have also led to much reduced noise levels. Sound intensity in this unit was not measured but it was quite unobtrusive in use, and no louder than a domestic refrigerator. In conclusion, this combined oxygen concentrator and ventilator driver satisfies the requirements for concentrations of oxygen greater than 21% for anaesthetic and therapeutic applications and is an acceptable alternative to a 100% oxygen supply. It can deliver up to 95% oxygen at low flows for air enrichment during anaesthesia or therapy and provides about 36% for use with a respirable gas ventilator. It is compact, quiet, reliable and, in combination with the Triservice apparatus, provides a highly versatile anaesthesia system.

Acknowledgments

The authors acknowledge Mr G. Weiss and Dr N.S. Jones of Kay Pneumatics Ltd, who designed and built the unit, Mr R. Madgwick and Mr P. Buchanan of the technical staff, Nuffield Department of Anaesthetics, for their assistance with measuring techniques, and the Director General, Medical Services, Royal Air Force, for permission to publish.

References

1. HOWELL RSC. Oxygen concentrators. *British Journal of Hospital Medicine* 1985; **40**: 221-3.
2. CARTER JA, BASKET PJF, SIMPSON PJ. The 'Permax' oxygen concentrator. *Anaesthesia* 1985; **40**: 460-5.
3. HARRIS CE, SIMPSON PJ. The 'Mini O₂' and 'Healthdyne' oxygen concentrators. *Anaesthesia* 1985; **40**: 1206-9.
4. WOOD PB. Oxygen concentrator in a remote hospital in Zaire. *Tropical Doctor* 1985; **15**: 26-7.
5. DOUGLAS GA, MERRIFIELD AJ. A combined oxygen concentrator and anaesthetic ventilator. *British Journal of Anaesthesia* 1986; **58**: 808.
6. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36**: 1094-1108.
7. DRAPER N, SMITH H. *Applied regression analysis*. New York: Wiley Interscience, 1981: 47-51, 108-115.
8. ROBINSON JS. An appraisal of piped medical gas systems. *British Journal of Hospital Medicine* 1982; **28**: 160-4.
9. EZI-ASHI TI, PAPWORTH DP, NUNN JF. Inhalational anaesthesia in developing countries. *Anaesthesia* 1983; **38**: 729-47.
10. MERRIFIELD AJ, DOUGLAS GA. Oxygen concentrators for casualties. *Fourth World Congress on Emergency and Disaster Medicine, Brighton, 4-7 June 1985. Section EE1, Aspects of aviation medicine*. World Association for Emergency and Disaster Medicine/British Association for Immediate Care, 1985: 77 (Abstract).
11. CHUSID EL. Oxygen concentrators. In: RENDELL-BAKER L, ed. *International anaesthesiology clinics, Vol. 20. Problems with anaesthetic and respiratory therapy equipment*. Boston: Little, Brown & Co., 1982: 235-47.

Some observations of levels of plasma cholinesterase activity within an obstetric population

M. WHITTAKER, J. S. CRAWFORD AND M. LEWIS

Summary

An account of plasma cholinesterase activity in samples of maternal and cord blood is presented. It is confirmed that plasma exchange markedly reduces the level of activity in maternal blood, and that the level is further reduced during the first 3-4 postnatal days. A particularly marked decrease was found in those cases in which spontaneous mid-trimester abortion occurred. The level of activity in maternal blood (excluding mothers subjected to plasma exchange) at the time of delivery, was higher than that in cord blood in 61% of cases. In 23% of cases the level of activity was appreciably (0.05 units) higher in cord blood, and two-thirds of these cord samples contained the E₂⁺ electrophoretic variant of plasma cholinesterase. The mean levels of activity in maternal and cord blood of Rhesus negative patients were significantly lower than those among Rhesus positive patients but there was no such distinction between Rhesus positive and Rhesus negative males and nonpregnant females. We encountered an incidence of 1:228 abnormal phenotypes in a series of 1593 mothers who underwent Caesarean section under a technique of general anaesthesia which included a suxamethonium infusion. However, probably only two of the seven patients would definitely be sensitive when not pregnant.

Key words

Anaesthesia; obstetric.
Enzymes; cholinesterase.

There is general agreement that a decrease in action of cholinesterase occurs during pregnancy.¹ The reason is unclear. The observation is particularly striking in view of the fact that the placenta contains a very small quantity of the enzyme; the cholinesterase in the placenta is predominantly acetylcholinesterase.² The associated reduction in enzymic activity is of no significance to maternal well-being under most circumstances, even when the mother receives suxamethonium. There are, however, some situations in obstetric practice in which the decrease in enzyme activity can, either by virtue of its superimposition upon an already low level or because it is exacerbated by other influences, be such as to render the mother particularly susceptible to suxamethonium.

We have been interested during the past few years in the collection of information that relates to plasma cholinesterase activity in selected groups of patients who attend this hospital, and we present here a summary of some of our findings.

Results

Plasma exchange

This hospital is a referral centre for cases of Rhesus iso-immunisation. Plasma exchange is a measure employed in the treatment of mothers whose infants are, or are likely to become, severely affected by the disease. The sequence of exchanges may start very early in pregnancy or be initiated in mid- or early third trimester, depending upon the presentation and progress of the maternal and fetal responses. One result of plasma exchange, as reported by Evans *et al.*,³ is a dramatic reduction in the level of maternal cholinesterase activity. We have studied 21 patients in this category during the past 3-4 years and the results fully confirm Evans and colleagues' findings.

There would be little merit in giving details here of the precise changes observed in each of the patients, since these depend to a considerable extent upon the frequency and number of plasma exchanges. Some general observations

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are, however, worthwhile. The level of activity decreases abruptly after the first exchange. Assays of blood obtained immediately before each subsequent exchange gave results that varied among patients from at least 0.20 to 0.40 units of activity below the pre-exchange value, considerably lower than the normal range during pregnancy. The individual levels of activity for each patient remained fairly constant throughout the period of gestation under review. Five of the 21 pregnancies ended in spontaneous abortion at 22–25 weeks' gestation, and it is interesting that the level of cholinesterase activity in each of these cases had decreased markedly, to 0.15, 0.21, 0.22, 0.22 and 0.27 units, respectively. The normal range is 0.80–1.20 units. We are reluctant to draw any conclusion from this observation but suggest that it be borne in mind.

The postnatal decrease in activity which is observed in normal pregnancy⁴ was also found in these cases, so that mothers who are subjected to plasma exchange must be assumed to be extremely enzyme deficient during the first 2–3 days after delivery. We have found that a relatively normal level of activity is regained only after 2–6 weeks following delivery in the few cases which we have been able to follow for longer than the immediate postpartum period.

Maternal and cord levels

We undertook a study of relative cholinesterase activity in maternal and cord blood in 74 cases in which the mother was Rhesus positive and of normal phenotype (Table 1). The range in the values obtained was considerable and probably reflects the flat Gaussian distribution curve of enzymic activities seen in a random population of this phenotype. The cholinesterase level in maternal blood may be an index of the well-being of the fetus. The mean value was slightly lower than those quoted by other authors (see Whittaker¹ for a review). As might have been anticipated, the route of delivery and whether or not the mother had received general anaesthesia, an epidural or neither, was not associated with a noteworthy difference in activity.

We made the arbitrary distinction that a difference of

0.05 units or less between maternal and cord values, represented equivalence. We determined on this basis that the maternal level was higher than that in the cord in 61% of cases, whereas the cord level was higher in 23%. It is known that the E_2^+ electrophoretic variant of plasma cholinesterase is associated with a 30% increase in enzymic activity when compared with the E_2^- variant.⁵ We showed by electrophoretic analysis that 67% of the cord blood with activity higher than the maternal sample had the E_2^+ variant. There was no incidence of E_2^+ when maternal and cord blood were effectively identical. We could not discover any factor which might consistently have led to a relatively increased maternal level. The range of values in cord blood was as wide as that in maternal blood, again an indication of the flat Gaussian distribution found in a random population.

Rhesus negative and Rhesus positive

Some observations made during the studies on patients who underwent plasma exchange suggested that Rhesus negative patients might have lower cholinesterase activity than normal before the series of exchanges was started. We therefore studied 52 mothers who were Rhesus negative, with normal genotype, who had not been treated by plasma exchange (Table 1). There appeared to be no significant difference in either maternal or cord levels, between the group which had Rh antibodies and the remainder. There was certainly a lower mean level of activity in the blood of Rhesus negative mothers than in those who were Rhesus positive ($p < 0.001$). The mean activity in cord blood from Rhesus negative cases was somewhat lower than that from Rhesus positive cases ($p < 0.01$). The level in maternal blood was higher (by at least 0.05 units) than that in cord blood in only 31% of Rhesus negative cases; the reverse was the case in 27%. We could think of no reason why there should be a relationship between cholinesterase activity and the Rhesus status of an individual which, if confirmed, would imply a linking of two separate genes. We therefore examined blood obtained from males and nonpregnant females of child-bearing age (excluding in-

Table 1. Mean values (and ranges) of cholinesterase activity (μmol benzoylcholine hydrolysed/minute/ml plasma) in blood sampled from mothers and umbilical cord. Also noted is the number of instances in which the level in maternal blood (M) was more than 0.05 units greater than that in cord blood (C), in which the contrary occurred, and in which the levels were within 0.05 units of each other.

	<i>n</i>	Maternal	Cord	M > C	C > M	M = C
<i>Rh negative</i>						
No antibodies	42	0.58 (0.40–0.91)	0.57 (0.33–0.93)	14	12	16
With antibodies	10	0.55 (0.38–0.75)	0.54 (0.32–0.75)	2	2	6
Total	52	0.58 (0.38–0.91)	0.57 (0.33–0.93)	16	14	22
<i>Rh positive</i>						
Caesarean section/general anaesthetic	25	0.70 (0.43–1.04)	0.60 (0.43–0.75)	18	5	2
Caesarean section/epidural	22	0.71 (0.47–1.08)	0.66 (0.35–1.02)	12	5	5
Vaginal delivery/epidural	18	0.66 (0.34–0.92)	0.58 (0.43–0.86)	11	5	2
Vaginal delivery/no epidural	9	0.68 (0.42–0.90)	0.65 (0.45–0.80)	4	2	3
Total	74	0.69 (0.34–1.08)	0.62 (0.35–1.02)	45	17	12

Table 2. Cholinesterase activity (μmol benzoylcholine hydrolysed/minute/ml plasma) in Rhesus positive and negative males and females.

Cholinesterase activity	Male		Female	
	Rhesus positive (n = 41)	Rhesus negative (n = 20)	Rhesus positive (n = 72)	Rhesus negative (n = 28)
Mean	0.956	0.936	0.816	0.808
Range	0.60–1.57	0.68–1.62	0.47–1.62	0.56–1.21

stances of abnormal cholinesterase genotypes) to test that unlikely hypothesis. The results are shown in Table 2.

The contrast derived from our series of pregnant subjects was manifestly spurious and there appears to be no direct relationship between cholinesterase activity and the Rhesus factor. The lower activity among the nonpregnant female population probably reflects the fact that many of the subjects probably took an oral contraceptive, a fact into which we did not enquire.

Abnormal phenotypes

It is not uncommon for us to encounter patients who take an unusually long time to recover from suxamethonium. In each of these instances a sample of maternal blood is obtained for analysis of cholinesterase activity, and again at the 6-week postnatal visit when, it is anticipated, the pregnancy induced depression of activity will have ended. During the past 12 years we have encountered at least 12 such mothers in whom phenotyping revealed a cholinesterase variant. We did not search for the records of all instances met with during that period. Of particular interest, however, is that seven mothers who underwent Caesarean section under general anaesthesia during the years 1983–85 had a prolonged recovery from suxamethonium and were subsequently found to have an abnormal genotype (Table 3). During that period 1593 mothers received general anaesthesia for Caesarean section. Relaxation throughout the operation was provided by an infusion of suxamethonium in all of these cases. The incidence of sensitivity to suxamethonium was thus 1:228, considerably higher than that usually quoted. This increased incidence possibly reflects the fact that we provide a suxamethonium infusion throughout the operative procedure, in contrast to the techniques applied in many other clinical services. We thus have the opportunity to identify, by clinical observations alone, the total number of our patients who exhibit

a delayed recovery from the effects of the drug. Peripheral nerve stimulation was not used as a monitoring device.

Discussion

Much can be learned from the simple accumulation of clinical data, possibly allied with a single, perhaps unusual, supplementary observation. We have confirmed the very low level of activity which results from plasma exchange, and observed that the reduction in activity which normally occurs during the few days after delivery is also seen in these patients, with the result that extremely low levels of activity can occur during that period. We have observed that there is a very wide range of cholinesterase activity among Rhesus positive women at term, that the mean level in this group is rather lower than reported previously, and that the level of activity in maternal blood is higher than in cord blood sampled at delivery in 61% of these cases.

Our investigation concerned an unselected series of 1593 cases of Caesarean section conducted under general anaesthesia (duration of operation 30–50 minutes), in which suxamethonium was the sole relaxant used (100 mg at induction, plus 200–400 mg by infusion). We observed seven instances (1:228) in which excessive delay in recovery of muscle power was subsequently shown to reflect an abnormal genotype. Such an incidence in a randomised population suggests that our commonly employed technique of general anaesthesia has disclosed evidence that the true incidence of abnormal genotypes is considerably greater than that usually quoted.

A good correlation between the duration of apnoea following suxamethonium and cholinesterase activity has been reported,⁵ although such a correlation has not been found in pregnant patients.^{6,7} The known decrease in enzymic activity associated with pregnancy could contribute to the number of individuals who become moderately sensitive to the drug during pregnancy. Such a situation is especially applicable to individuals who have one of the rare cholinesterase variants with lower mean activity than the usual phenotype. Of the seven sensitive patients in this study only one, of genotype E₁^a E₁^a, would definitely be sensitive to suxamethonium on all occasions. In addition, of the four patients with genotype E₁^a E₁^a (or E₁^k), one is known to be sensitive on all occasions and the other three could well be so. The other patients are heterozygotes and have one E₁^a gene; such individuals would not be expected to be sensitive to the drug. However, Viby Mogensen,⁸ who was able to predict the duration of apnoea following a single dose of suxamethonium (1 mg/kg) from cholinesterase activity, showed that 50% of E₁^a E₁^a heterozygotes will have a moderately prolonged reaction to the drug and 10% of these individuals will not have normal muscle transmission for 20 minutes. All the variants in our study are heterozygotes but the duration of apnoea is inversely

Table 3. Cases of sensitivity to suxamethonium encountered in patients who underwent Caesarean section under general anaesthesia during the period 1983–85. Except in the case identified in the table, each patient received 300–400 mg suxamethonium by intravenous infusion additional to the induction dose of 100 mg.

Genotype	Cholinesterase activity	Duration of postoperative apnoea (minutes)
E ₁ ^a /E ₁ ^a	0.38	45
E ₁ ^a /E ₁ ^a	0.07	35
E ₁ ^a /E ₁ ^a	0.10	+ 30
E ₁ ^a /E ₁ ^{u or k}	0.69	10
E ₁ ^a /E ₁ ^{a or k}	0.55	known sensitivity, 100 mg suxamethonium
E ₁ ^a /E ₁ ^a	0.07	30
E ₁ ^a /E ₁ ^a	0.19	180

related to cholinesterase activity for the two $E_1^a E_1^a$ individuals. The increased frequency of suxamethonium sensitivity found in this study supports the hypothesis that heterozygotes become more susceptible to suxamethonium during pregnancy.

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References

1. WHITTAKER M. Plasma cholinesterase variants and the anaesthetist. *Anaesthesia* 1980; **35**: 174-97.
2. ORD MG, THOMPSON RHS. Nature of placental cholinesterase. *Nature* 1980; **165**: 927-8.
3. EVANS RT, MACDONALD R, ROBINSON A. Suxamethonium apnoea associated with plasmapheresis. *Anaesthesia* 1980; **35**: 198-201.
4. ROBSON N, ROBERTSON I, WHITTAKER M. Plasma cholinesterase changes during the puerperium. *Anaesthesia* 1986; **41**: 243-9.
5. WHITTAKER M. Cholinesterase. In: BECKMAN L, ed. *Monographs in human genetics, Vol. II*. Basel: Karger, 1986: T-125.
6. HUNTER AR. Suxamethonium apnoea. A study of eighteen cases. *Anaesthesia* 1966; **21**: 325-36.
7. BLITT CD, PETTY WC, ALBERTERNST EE, WRIGHT BJ. Correlation of plasma cholinesterase activity and duration of action of succinylcholine during pregnancy. *Anesthesia and Analgesia* 1977; **56**: 78-83.
8. VIBY-MOGENSEN J. Succinylcholine neuromuscular blockade in subjects heterozygous for abnormal plasma cholinesterase. *Anesthesiology* 1981; **55**: 231-5.

Forum

Total intravenous anaesthesia for military surgery. A technique using ketamine, midazolam and vecuronium

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Summary

Ketamine and midazolam were used for induction of anaesthesia and by continuous intravenous infusion for maintenance to assess their suitability for use in a total intravenous anaesthetic technique in the management of battle casualties. Muscular relaxation was provided by vecuronium and the patients' lungs ventilated with air. Ketamine was infused at a rate of 2 mg/kg/hour. This was achieved by mixing ketamine 200 mg, midazolam 5 mg and vecuronium 12 mg in 50 ml normal saline. The rate of infusion of the mixture (ml/hour) was then equal to 50% of the body weight in kg. The technique proved to be simple, effective and versatile and should be adaptable for use in the management of battle casualties.

Key words

Anaesthetic techniques; infusion.
Hypnotics; midazolam.

The overriding principle of military surgery is the delayed primary suture of wounds. Therefore, by definition, battle casualties will receive more than one anaesthetic for the treatment of their injuries. The use of the Triservice anaesthetic apparatus (TSA) has been well tried and documented.^{1,2} It is a drawover system that uses ambient air as the primary carrier gas, and halothane and trichloroethylene as the volatile anaesthetic agents.

However, in view of current opinions about liver damage due to repeated halothane anaesthetics,³ it would be preferable if this agent were not used in the first instance. In addition, the manufacture of trichloroethylene has been threatened in the past and the future production of this agent cannot be guaranteed. The use of the newer inhalational agents, enflurane and isoflurane, has been recommended.⁴ Unfortunately, enflurane, which does have analgesic properties,⁵ has a high MAC and isoflurane, at present, is very expensive.

We felt that a total intravenous technique is an obvious alternative in the treatment of battle casualties. This study was therefore designed to assess the suitability of such a technique using a mixture that contained ketamine, midazolam and vecuronium, accurately delivered intravenously by means of a syringe pump. Ketamine has been used widely as the induction and maintenance drug of choice for trauma cases but the high incidence of unpleasant side effects has limited its acceptance. Vecuronium bromide, one of the more recently introduced non-depolarising muscle relaxants, has been used because it is available as an anhydrous powder and therefore stores well. Vecuronium is free of adverse circulatory effects and the incidence of release of histamine is minimal.⁶

It is our contention that all battle casualties will have a

full stomach, irrespective of the interval between time of injury and time of surgery. Therefore, tracheal intubation is mandatory and intermittent positive pressure ventilation can be used for the duration of the surgical procedure. Another essential requirement for war surgery is that patients should recover quickly and be able to maintain a clear airway as soon as possible.

Methods

One hundred patients, 36 male and 64 female, age range 16–50 years, who presented for elective abdominal, thoracic or body surface surgery at this hospital were studied. All patients were in ASA classes 1 and 2. It was estimated that their operations would last at least 45 minutes. Patients with a past medical history of psychiatric illness, with hypertension and those with a history of a previous cerebrovascular accident were not studied.

All patients were seen pre-operatively. The following details were recorded: initials, sex, body weight, relevant medical history and physical findings. All were premedicated with papaveretum and hyoscine one hour pre-operatively. Monitoring of the electrocardiogram and blood pressure (Dinamap) was commenced on arrival in the anaesthetic room and a vein on the dorsum of the hand or forearm was cannulated. Systolic, diastolic and mean arterial pressure and pulse rate were recorded 5 minutes before induction and at 3–5-minute intervals thereafter.

Anaesthesia was induced with midazolam 0.07 mg/kg followed 2 minutes later by ketamine 1.0 mg/kg and vecuronium 0.1 mg/kg, and maintained by constant infusion of a mixture of the same three drugs using an electrically driven syringe pump (IMED 800) at the following rates:

midazolam 50 µg/kg/hour, ketamine 2.0 mg/kg/hour and vecuronium 120 µg/kg/hour. This mixture is obtained by mixing midazolam 5 mg, ketamine 200 mg and vecuronium 12 mg and making up to 50 ml with normal saline. A convenient *aide memoire* to the rate of administration of this mixture is:

$$\frac{\text{patient's body weight in kg}}{2} = \text{ml/hour}$$

The patient's lungs were ventilated with oxygen-enriched air, with an FIO_2 of 0.35, tidal volume 10 ml/kg at a respiratory rate of 12 breaths/minute using a Penlon Oxford ventilator. In 10% of cases the end tidal carbon dioxide was monitored by capnography (Datex) and the efficacy of neuromuscular blockade was assessed with a peripheral nerve stimulator (Datex Relaxograph) that delivered train-of-four stimuli to the ulnar nerve.

The infusion was stopped 10–15 minutes prior to the end of surgery and residual neuromuscular blockade reversed with either atropine and neostigmine, or glycopyrronium and neostigmine. The times of relaxant reversal and tracheal extubation and the time at which the patient regained consciousness in the recovery area were recorded. The latter was when the patient was able to give name, military number (where appropriate) and ward number. The patient's behaviour in the recovery area was recorded as either satisfactory or unsatisfactory. Specific problems were recorded in the case of the latter.

All patients were visited 24 hours postoperatively and questioned with regard to awareness during the operative procedure, the occurrence of dreams or hallucinations, and the occurrence of nausea or vomiting. The time from reversal to the first dose of narcotic was noted from the nursing Kardex.

Results

The types of operation performed are shown in Table 1. The details of the patients' age and weight are given in Table 2, and the duration of anaesthesia, total volume of infusate, and extubation to awakening time in Table 3. No patient complained of pain on injection of the drugs and induction of anaesthesia was very smooth; no excitatory phenomena were noted. The mean duration of anaesthesia was 73.6 minutes and the mean volume of infusate administered was 33.7 ml. The mean time from tracheal extubation to awakening was 12.5 minutes.

Cardiovascular effects. Some cardiostimulatory action was observed in all patients. Figure 1 shows the mean heart rate and Fig. 2 the mean systolic and diastolic blood pressures. There was an initial increase in heart rate and arterial blood pressure associated with tracheal intubation. The heart rate and blood pressure began to decrease after 5 minutes and had returned to pre-operative levels by 30 minutes. At no time was the arterial blood pressure lower than the level prior to induction of anaesthesia (Table 4).

Recovery. None of the patients in this study was aware during the operative period and all but one said that they would be perfectly happy to have the same anaesthetic again. This patient suffered nightmares but had had a similar experience after a previous general anaesthetic when thiopentone, nitrous oxide, oxygen and halothane were used. The behaviour of all the patients was rated to be entirely satisfactory by the recovery nursing staff. They were not nursed in silence or darkness. Two patients were given perphenazine 5 mg for nausea and two were given doxapram 50 mg to stimulate respiration.

The incidence of postoperative dreaming was 15%; five patients complained that the dreams were unpleasant. Post-

Table 1. Types of operation performed.

	Male	Female
Abdominal hysterectomy	—	19
Vaginal hysterectomy	—	12
Laparotomy	2	15
Other gynaecological operations	—	5
Thoracotomy	4	—
Upper abdominal surgery	6	5
Varicose veins	4	5
Herniorrhaphy	8	—
Orthopaedic procedures	8	2
Others	4	1
Total	36	64

Table 2. Mean (SEM) and range of age and weight of patients.

	n	Age, years	Range	Weight, kg	Range
Male	36	29.6 (8.6)	17–49	76.2 (11.4)	51–97
Female	64	35.8 (7.5)	19–49	62.3 (8.6)	42–82

operative vomiting occurred in only one male patient (2.8%) and in 24 female patients (37.5%). Seventy-eight of the patients required postoperative analgesia; the mean time of administration of the first dose was just over 4.5 hours after extubation.

Discussion

The concept of a total intravenous anaesthetic technique for war surgery is attractive but it suffered a severe setback at Pearl Harbour. Thiopentone was used as the sole agent and lack of knowledge of its cardiovascular and respiratory depressant effects led to disastrous consequences. Halford⁷ stated that intravenous anaesthesia is an ideal method of euthanasia.

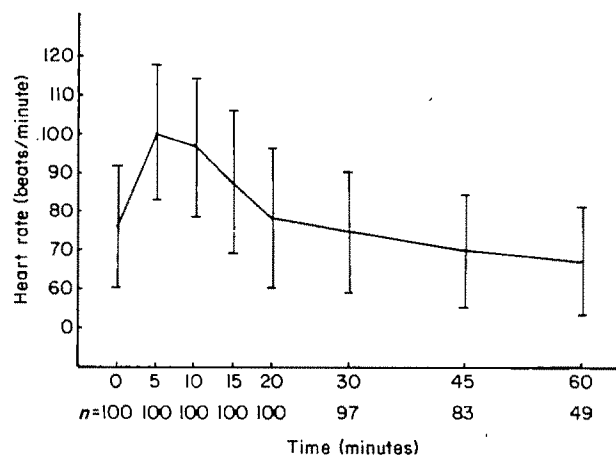
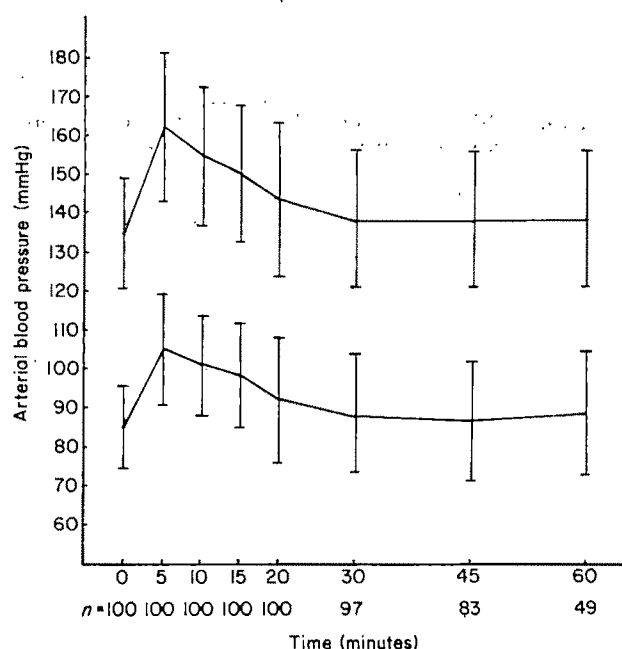
When we decided to examine again a total intravenous technique for war injuries we had three objectives: firstly, to find a safe and simple method to anaesthetise battle casualties in such a way that they are in the best possible condition for surgery, asleep, relaxed and with reflexes suppressed; secondly, to develop a technique which ensures that patients awaken rapidly postoperatively and are able to maintain a safe airway; and thirdly, to develop a technique that can be supervised safely by paramedical personnel.

We chose three drugs which are all water soluble and can be mixed together without any precipitation. They would appear to be stable in solution and the mixture can be used at least 72 hours after preparation. The individual drugs have a long shelf-life and do not need to be stored in a refrigerator. Pharmacokinetically the combination of ketamine and midazolam is attractive. The distribution half-life of both drugs is 10–15 minutes, the elimination half-life of ketamine is 2.5–3.1 hours and of midazolam 1.5–2.5 hours. The clearance of ketamine is 18.0 ml/kg/minute and of midazolam, 8.1 ml/kg/minute. When midazolam is mixed with ketamine, which has pH 3.5–5.5, the open ring configuration of the former drug outside the body is maintained.

Ketamine is a controversial drug. The slow onset of action, its relatively prolonged duration, together with the high incidence of adverse reactions during recovery, seem to make it unsuitable for continuous intravenous infusion.⁸ The emergence phenomena consist of dreams, pleasant and unpleasant, and disturbance of sensory perception. Various methods have been tried to overcome emergence phenomena: patient selection, heavy opioid premedication,⁹ benzodiazepine combinations, diazepam,¹⁰ lorazepam,¹¹ fluni-

Table 3. Mean (SEM) and range of duration of anaesthesia, recovery time and total volume of infusate.

	<i>n</i>	Duration of anaesthesia, minutes	Range	Tracheal extubation-awakening, minutes	Range	Total volume of infusate, ml	Range
Male	36	94.5 (55.4)	25-281	11.8 (12.1)	1-60	50.7 (37.7)	8-194
Female	64	61.9 (19.4)	30-119	12.8 (15.5)	1-92	24.1 (10.4)	7-51

**Fig. 1.** Mean (SEM) changes in heart rate.**Fig. 2.** Mean (SEM) changes in systolic and diastolic blood pressure.

trazepam¹² and isolation of the patient from extraneous stimuli. The combination of midazolam with ketamine has been recommended previously.¹³ The ideal intravenous anaesthetic is not available but this combination possesses mutually complementary pharmacological properties.¹⁴

We used a very low total dosage of ketamine in this study and this, together with continuous administration of midazolam, probably accounts for the almost total absence of emergence phenomena. The advantages of ketamine are exploited in this technique. The cardiovascular system is supported and this would be beneficial in the treatment of hypovolaemic battle casualties. Unlike most other methods of anaesthesia the arterial blood pressure does not decrease following induction. Airway maintenance was

Table 4. Mean (SEM) increases or decreases (–) in heart rate and systolic arterial pressure.

Time, minutes	Heart rate, beats/minute	Systolic arterial pressure, mmHg
5	22.2 (17.3)	27.4 (19.2)
10	21.4 (18.1)	20.0 (18.1)
15	11.6 (18.7)	15.9 (17.5)
20	2.6 (18.0)	9.0 (19.7)
30	–0.6 (15.3)	3.2 (17.5)
45	–5.7 (14.6)	3.4 (17.3)
60	–8.5 (14.0)	4.0 (17.7)

satisfactory postoperatively, patient acceptability was high and there were no cases of awareness. The fact that there is no simple, reliable and objective index that indicates awareness during anaesthesia is probably the single most restricting factor in the use of a total intravenous technique with relaxant drugs.⁸

Midazolam has proved to be the ideal benzodiazepine for use in this field.¹⁵ It is water soluble, mixes with the other drugs and does not cause phlebitis. It provides good anterograde amnesia and, unlike the earlier benzodiazepines, has no second peak effect. It should be noted that the benzodiazepines lose potency when mixed with Hartmann's solution, and normal saline should be used for the preparation of this mixture.

Vecuronium is the non-depolarising muscle relaxant with the least adverse side effects. Histamine release is minimal, the breakdown products are innocuous, it is cardiostable and does not produce tachycardia even though it is a derivative of pancuronium. The fact that vecuronium is prepared as an anhydrous powder is most useful to us since it stores well, has a long shelf-life and does not require refrigeration.

The changes in heart rate and blood pressure found in this study were similar to those found by Lilburn *et al.*¹⁶ using tubocurarine. The haemodynamic response to intubation is well documented;¹⁷ midazolam does give protection but in much larger doses.¹⁸ It is doubtful if midazolam has much effect on the cardiostimulatory action of ketamine or the plasma catecholamine level. We feel that the tachycardia and hypertension are acceptable in the management of the previously fit soldier, aged 18–45 years whose cardiovascular system will withstand swings in pulse rate and arterial blood pressure. There were no instances of unusual cardiac dysrhythmias.

Recovery, as evidenced by the tracheal extubation to awakening time, was fairly rapid and emergence was smooth. The mean awakening time (12.5 minutes) would have been even shorter had not three cases taken over 60 minutes to recover. Swift recovery is particularly important in the military context. In a combat area there will be a shortage of skilled anaesthetists and nurses; therefore, patients must recover consciousness and reflexes quickly. There is likely to be a limited postoperative holding capability and casualties may have to be evacuated early. Postoperative behaviour was normal in all patients despite the absence of special precautions such as silence and darkness.

The incidence of nausea and vomiting was no higher than

that found using any other technique and compares favourably with a previous report.¹⁹ The much higher incidence in the females was probably due to the nature of the surgery. Many of the patients who vomited had done so previously after a conventional technique had been used.

Early observations suggested that analgesia following ketamine administration outlasted the period of anaesthesia and that this analgesic effect occurred at even subanaesthetic doses of ketamine. In this series the mean time from extubation to the administration of the first dose of post-operative analgesia was 272 minutes. We do not feel that any conclusions can be drawn from this observation about the duration of the analgesic effect of ketamine. However, only one patient required postoperative analgesia whilst still in the recovery area. This factor must have been significant in the smooth emergence of these patients from anaesthesia.

It is unlikely that battle casualties will be premedicated with papaveretum and hyoscine. Previous experience has shown that casualties will receive doses of analgesic on the battlefield and in transit to the field hospital.² At present, the drug that the injured are likely to receive is papaveretum and that is why this drug was chosen as the premedicant. If necessary, supplements of analgesic can be given at the time of induction or during the procedure. Suxamethonium was not used for intubation but when casualties are treated it can be used for a crash induction followed by a loading dose of vecuronium in the normal way.

We do not recommend that this technique be adopted to the exclusion of all others in military surgery but we believe that it can be used to advantage when inhalational agents are not available or are not the most suitable agents. This method is simple, effective, versatile and can be used in combination with other techniques. It is cheap and effective, with air as the carrier gas. Once established, minimum monitoring and minimum interference are required. In conclusion, we believe that there is a place for total intravenous anaesthesia in the treatment of battle casualties and that the technique that we have described will prove to be significant and safe.

References

- HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36**: 1094–1108.
- JOWITT MD, KNIGHT RJ. Anaesthesia during the Falklands campaign. *Anaesthesia* 1983; **38**: 776–83.
- BLOGG CE. Halothane and the liver: the problem revisited and made obsolete. *British Medical Journal* 1986; **292**: 1691–2.
- TIGHE SQM. An ideal agent for drawover anaesthesia? *Anaesthesia* 1986; **41**: 1160–1.
- MCGUINNESS C, ROSEN M. Enflurane as an analgesic in labour. *Anaesthesia* 1984; **39**: 24–6.
- CRUL JF, BOOI LHDJ. First clinical experiences with Org NC45. *British Journal of Anaesthesia* 1980; **52**: 49S–52S.
- HALFORD FJ. A critique of intravenous anaesthesia in war surgery. *Anesthesiology* 1943; **4**: 67–9.
- MORGAN M. Total intravenous anaesthesia. *Anaesthesia* 1983; **38** (Suppl.): 1–9.
- LILBURN JK, DUNDEE JW, NAIR SG, FEE JPH, JOHNSTON HML. Ketamine sequelae. Evaluation of the ability of various premedicants to attenuate its psychic actions. *Anaesthesia* 1978; **33**: 307–11.
- BOVILL JG, CLARKE RSJ, DUNDEE JW, PANDIT SK, MOORE J. Clinical studies of induction agents. XXXVIII. Effect of premedicants and supplements on ketamine anaesthesia. *British Journal of Anaesthesia* 1971; **43**: 600–8.
- LILBURN JK, DUNDEE JW, MOORE J. Lorazepam–ketamine: preliminary report. *British Journal of Anaesthesia* 1976; **48**: 1125.
- HOULTON PJC, DOWNING JW. General anaesthesia with intravenous flunitrazepam, continuous ketamine infusion and muscle relaxant. A preliminary report. *South African Medical Journal* 1978; **54**: 1048–9.
- WHITE PF, WAY WL, TREVOR AJ. Ketamine – its pharmacology and therapeutic uses. *Anesthesiology* 1982; **56**: 119–36.
- WHITE PF. Comparative evaluation of intravenous agents for rapid sequence induction – thiopental, ketamine, and midazolam. *Anesthesiology* 1982; **57**: 279–84.
- CARTWRIGHT PD, PINGEL SM. Midazolam and diazepam in ketamine anaesthesia. *Anaesthesia* 1984; **39**: 439–42.
- LILBURN JK, DUNDEE JW, MOORE J. Ketamine infusions. Observations on technique, dosage and cardiovascular effects. *Anaesthesia* 1978; **33**: 315–21.
- LOW JM, HARVEY JT, PRYS-ROBERTS C, DAGNINO J. Studies of anaesthesia in relation to hypertension. VII. Adrenergic responses to laryngoscopy. *British Journal of Anaesthesia* 1986; **58**: 471–7.
- BORALESSA H, SENIOR DF, WHITWAM JG. Cardiovascular response to intubation. A comparative study of thiopentone and midazolam. *Anaesthesia* 1983; **38**: 623–7.
- JAGO RH, RESTALL J. Postoperative dreaming. A comparison of the incidence following pentazocine and morphine premedication. *Anaesthesia* 1983; **38**: 438–41.

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Temazepam and recovery in day surgery

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Summary

A double-blind trial of temazepam premedication for day cases was undertaken. Effective anxiolysis was recorded in the groups that received temazepam 10 or 20 mg and there was no prolongation of delayed recovery times as measured by memory test cards. All patients were discharged from the day unit 3 hours after the administration of general anaesthesia.

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Key words

Anaesthesia; outpatient.
Hypnotics, benzodiazepines; temazepam.

Increased interest in day surgery in this country has focused attention on anaesthetic agents with a rapid onset of action and swift recovery to street fitness. Pre-operative medication is frequently omitted in day case anaesthesia on the grounds that it is unnecessary,¹ may prolong recovery time² or put patients at risk after they are discharged from hospital.³

The benzodiazepine temazepam has a rapid onset of action: peak plasma levels are attained within 40 minutes of oral administration. It has a short duration of action, produces no pharmacologically active metabolites⁴ and has been proposed as a suitable premedicant for day patients.^{3,5} Increased appreciation of the anxiety experienced by many of our patients who present for vaginal termination of pregnancy, prompted us to investigate the use of temazepam in this group of patients and to assess their return to street fitness.

Methods

The study was approved by the District Ethical Committee and informed consent was obtained from all the participants. Sixty healthy day patients scheduled for vaginal termination of pregnancy were studied, aged 16–45 years, weight 50–80 kg and with no history of psychiatric, renal or hepatic disease. Any patients regularly taking anxiolytic or psychotherapeutic drugs were not included in the trial.

The 60 patients were randomly allocated to three groups

of 20 each and, following a pre-operative anaesthetic assessment visit, each was given a capsule of premedication orally: this was either 10 or 20 mg temazepam or a placebo. The premedication was timed to be given approximately one hour pre-operatively and the study was designed on a double-blind basis.

All patients received a general anaesthetic from one of the authors (T.W.O.) which consisted of intravenous alfentanil 7 µg/kg followed by methohexitone 1.5 mg/kg and spontaneous ventilation with 70% nitrous oxide in oxygen using a Bain breathing system, with increments of methohexitone 0.25 mg/kg as required.

A 100-mm visual analogue scale was used to assess anxiety^{6,7} on admission to the trial, immediately pre-operatively and again at 1 and 2 hours postoperatively. Early recovery was assessed by the recovery nursing staff using Steward's recovery score, and delayed recovery was monitored by one of the authors (P.A.O.) using Bethune's modification of the William's delayed recall test.^{8–10} Any side effects observed or volunteered by the patients in the recovery ward were noted.

Probability values were obtained from analysis of variance *F*-statistics using 2 and 57 degrees of freedom where three groups of patients were compared. When only two groups were compared, two-sample *t*-tests on 58 degrees of freedom were used.

Results

Table 1 shows the mean ages, weights, total doses of methohexitone given, duration of anaesthesia and immediate recovery times in the series. There were no significant differences in the demographic data.

Table 1. Mean (SD) ages, weights, total doses of methohexitone, durations of anaesthesia and immediate recovery times.

	Placebo (n = 20)	Temazepam 10 mg (n = 20)	Temazepam 20 mg (n = 20)	p *
Age, years	26.7 (7.7)	23.4 (8.0)	24.5 (6.7)	0.37
Weight, kg	64.2 (10.8)	61.4 (6.5)	64.2 (8.4)	0.52
Methohexitone, mg/kg	3.0 (0.3)	3.1 (0.4)	3.1 (0.4)	0.75
Duration of anaesthesia, minutes	7.1 (1.6)	7.0 (1.8)	7.3 (2.4)	0.87
Immediate recovery time, minutes	5.7 (3.2)	8.7 (6.0)	8.8 (4.9)	0.08

* Values of p compare the three groups simultaneously.

Table 2. Mean (SD) visual analogue scores for anxiety.

	Placebo	Temazepam 10 mg	Temazepam 20 mg	p *
Admission	40.5 (23.5)	52.6 (20.1)	50.7 (21.7)	0.18
Immediately pre-operatively	47.1 (23.0)	47.0 (19.5)	31.3 (18.0)	0.02
1 hour postoperatively	23.3 (27.2)	24.8 (19.9)	23.8 (23.4)	0.98
2 hours postoperatively	11.9 (19.1)	10.3 (16.1)	13.1 (20.5)	0.90
Pre-operative-admission	6.7 (25.2)	-5.6 (21.3)	-19.5 (26.1)	0.005

* Values of p compare the three groups simultaneously.

Table 3. Mean (SD) memory function scores. Negative values denote errors in recall.

	Placebo	Temazepam 10 mg	Temazepam 20 mg	p *
<i>New facts</i>				
Pre-operatively	-5.1 (4.8)	-6.2 (4.4)	-8.2 (4.6)	0.11
1 hour postoperatively	-10.7 (6.6)	-12.0 (6.2)	-13.9 (5.6)	0.26
2 hours postoperatively	-6.4 (6.5)	-6.9 (4.7)	-9.2 (4.9)	0.24
<i>Reinforcement</i>				
Pre-operatively	-6.6 (5.1)	-8.4 (5.7)	-9.9 (5.0)	0.13
1 hour postoperatively	-3.6 (4.2)	-3.8 (3.4)	-7.5 (4.2)	0.003
2 hours postoperatively	-1.9 (2.6)	-3.8 (3.1)	-3.3 (2.9)	0.10

* Values of p compare the three groups simultaneously.

Table 4. Mean (SD) analysis of anxiety scores. Patients in all study groups placed according to age and marital status: group A, younger than 22 years and unmarried ($n = 31$); group B, older than 22 years and married ($n = 29$).

	Group A	Group B	p*
Admission	49.0 (21.4)	46.7 (23.2)	0.70
Pre-operatively	48.5 (19.0)	34.4 (21.5)	0.01
1 hour postoperatively	30.5 (25.9)	17.0 (18.2)	0.02
2 hours postoperatively	17.0 (22.0)	6.1 (11.4)	0.02

* Values of p compare the three groups simultaneously.

Table 2 records the visual analogue scores for anxiety. Immediately before induction of anaesthesia the temazepam 20 mg group scored significantly less anxiety than the other two ($p = 0.02$). The pre-operative-admission score demonstrates that the anxiety level of the placebo group increased whilst patients awaited surgery, whereas that of the two temazepam groups decreased over this period ($p = 0.005$). These differences were no longer apparent at 1 and 2 hours into the postoperative period.

Table 3 shows the memory test results for longer term recovery in the series. Memory for new facts was impaired at one hour in all groups but had returned almost to pre-operative values by 2 hours postoperatively, and differences between the groups did not reach statistical significance. The temazepam 20 mg group had significantly more errors in recall of old facts at one hour ($p = 0.003$) but the trend in all groups was for less errors with increase in post-operative time, and by 2 hours the difference was no longer significant.

Discussion

Anaesthetists vary in their approach to the relief of pre-operative anxiety prior to day surgery. The important questions in the present study were whether patients were subjectively helped by premedication, and whether their return to street fitness was compromised by an anxiolytic agent. Patients scheduled for the termination of pregnancy frequently display high anxiety levels, a clinical impression borne out by our admission visual analogue scores. When all 60 patients were divided into two groups according to age and marital status, as shown in Table 4, the anxiety scores demonstrated that the younger unmarried patients whose anxiety on admission was comparable with that of the older, married group, were thereafter significantly more anxious, a difference that persisted 2 hours postoperatively. This finding taken together with our demonstration of a decrease in anxiety following temazepam premedication, has obvious implications for the management of anaesthesia in this group of patients. No physiological measurements of anxiety were made but the anaesthetist (T.W.O.) correctly estimated in 70% of cases whether or not temazepam had been given.

Memory function has been shown to be a reliable indicator of long-term recovery following general anaesthesia.¹¹ Memory was again impaired in this series, a result consistent with the combined effect of premedication and anaesthesia. The pharmacokinetics of temazepam suggest that its contribution to memory impairment has decreased 2 hours into the postoperative period. Anxiety in itself may impair memory, as general anaesthesia has been shown to do. Temazepam has been shown not to have a late re-onset effect, and three previous studies that investigated the use of premedication for minor and day surgery also suggested that it is the logical drug to use.^{3,5,12} Immediate recovery

was shorter in our placebo group of patients but we consider longer term recovery to be more relevant in the context of day surgery.

The logistics of managing a group of premedicated day patients were not a problem. As the study progressed we found it easier to allow those patients who became drowsy pre-operatively to stay on their trolleys in the ward area, while those who were alert sat with other patients in the waiting room and then walked with supervision to the operating theatre. Eight patients were drowsy pre-operatively, seven after temazepam and one after placebo, and of the five patients drowsy one hour postoperatively, four had been given temazepam; the one patient drowsy 2 hours postoperatively had received the placebo. Four patients, three of whom had taken temazepam, volunteered that the preparation had helped them. Nausea and vomiting had a similar incidence in all groups; vomiting was more frequent in those patients who were given Syntocinon pre-operatively. All patients were discharged home from the unit approximately 3 hours postoperatively; none was admitted as an inpatient during the course of the study.

In conclusion, the results of this study demonstrate that the use of temazepam in a day surgery unit may significantly reduce anxiety levels without prolonging the recovery period in this group of patients. Every patient was fit for discharge from the unit 3 hours postoperatively and was accompanied home by a responsible adult. Temazepam has been shown to be an effective anxiolytic for day cases and is the premedicant of choice for these patients in the Cambridge Day Surgery Unit.

Acknowledgment

We thank Sister D.R. Sutherland and the staff of Addenbrooke's Hospital Day Surgery Unit for their help with this study.

References

- MIRAKHUR RK, DUNDEE JW, CONNOLLY JDR. Studies of drugs given before anaesthesia. XVII. Anticholinergic premedicants. *British Journal of Anaesthesia* 1979; **51**: 339-45.
- BURN JMB. A blueprint for day surgery. *Anaesthesia* 1979; **34**: 790-805.
- AMARASEKERA K. Temazepam as a premedicant in minor surgery. *Anaesthesia* 1980; **35**: 771-4.
- Proceedings of a symposium on temazepam and related 1,4-benzodiazepines. British Journal of Clinical Pharmacology* 1979; **8** (Suppl. 1).
- BEECHY APG, ELTRINGHAM RJ, STUDD C. Temazepam as premedication in day surgery. *Anaesthesia* 1981; **36**: 10-15.
- MAXWELL C. Sensitivity and accuracy of the visual analogue scales. *British Journal of Clinical Pharmacology* 1978; **6**: 15-24.
- FISHER AP, VINE P, WHITLOCK J, HANNA M. Buccal morphine premedication. A double-blind comparison with intramuscular morphine. *Anaesthesia* 1986; **41**: 1104-11.
- STEWART DJ. A simplified scoring system for the postoperative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-3.
- WILLIAMS M. The measurement of memory in clinical practice. *British Journal of Sociology and Clinical Psychology* 1968; **7**: 19-34.
- BETHUNE DW. Test of delayed memory recall suitable for assessing postoperative amnesia. *Anaesthesia* 1981; **36**: 942-8.
- OGG TW, FISCHER HBJ, BETHUNE DW, COLLIS JM. Day case anaesthesia and memory. *Anaesthesia* 1979; **34**: 748-9.
- GREENWOOD BK, BRADSHAW EG. Preoperative medication and day case surgery. A comparison between oxazepam and temazepam. *British Journal of Anaesthesia* 1983; **55**: 933-6.

Hypoxaemia after premedication in cardiac patients. Glycopyrronium compared with hyoscine

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Summary

Arterial blood gases were analysed before and approximately one hour after premedication in two groups of 10 patients awaiting cardiac surgery. One group received intramuscular papaveretum and hyoscine, the other papaveretum and glycopyrronium. Similar, small but statistically significant reductions in mean arterial oxygen tension and oxygen saturation, and increases of arterial carbon dioxide tension occurred in both groups. Hypoxaemia in individual patients was unpredictable and in some was clinically relevant.

Key words

Complications; hypoxaemia.

Premedication; papaveretum, hyoscine, glycopyrronium.

Glycopyrronium is an anticholinergic drug with a structure that contains a quaternary ammonium group. This renders it highly ionised at body pH and effectively unable to cross the blood–brain barrier.¹ In studies of its use as a premedicant drug it has been found to produce less sedation than hyoscine, less visual disturbance than atropine, fewer dysrhythmias at the time of induction of anaesthesia than either, and to possess an antisialogogue effect similar to both.² Mirakhur *et al.*³ found that a dose of 0.2 mg was effective as premedication in adults.

Patients who present for coronary revascularisation are given sedative premedication primarily to avoid the haemodynamic consequences of pre-operative anxiety. The effect of intramuscular morphine or papaveretum combined with hyoscine is considered to be satisfactory in this respect.⁴ However, the administration of morphine with hyoscine to patients before coronary revascularisation, has been reported to reduce arterial oxygen tension (P_{aO_2}) to a degree sufficient to cause concern in half the patients studied; this effect was not observed after the administration of morphine alone.⁵

The effect on arterial blood gas values of the combination of papaveretum and glycopyrronium was therefore compared with that of papaveretum and hyoscine in order to determine whether post-premedication hypoxaemia might be avoided using an antisialogogue without central action.

Methods

Twenty men who presented for coronary revascularisation were studied. Patients with functional respiratory disease and those who required glyceryl trinitrate preparations in the hour before surgery were excluded. They were allocated randomly to receive either hyoscine 0.3 or 0.4 mg, or glycopyrronium 0.2 mg, with papaveretum 15 or 20 mg by intramuscular injection one hour pre-operatively; those who weighed less than 70 kg received the lower doses. All

patients received lorazepam 2 mg orally as night sedation on the previous evening, and maintenance β -adrenergic or calcium antagonist therapy was continued on the day of operation. A baseline blood gas sample was taken the day before surgery, under local anaesthesia from the radial artery after a rest period in bed of at least 10 minutes. A pre-induction arterial blood gas sample was taken one hour after premedication when the patient arrived on his ward bed in the anaesthetic room. All patients breathed air at the times of sampling.

Arterial blood samples were analysed immediately or stored on ice and analysed within one hour, using an ABL1 automated blood gas analyser (Radiometer, Copenhagen). Student's *t*-test was used to assess the significance of differences between blood gas data.

The anaesthetist in charge, who was unaware of the type of premedication administered, recorded the incidence of nausea or chest pain, the heart rate and rhythm and an assessment of the degree of sedation ('wakeful' or 'drowsy'). Following tracheal intubation, he recorded the state of the airway as 'wet' or 'dry'.

Results

The two groups were similar in respect of age and weight; 53.7 years (SEM 1.6) and 71.1 kg (SEM 4.8) in the hyoscine group, and 53.7 years (SEM 2.5) and 76.5 kg (SEM 3.7) in the glycopyrronium group. There were no significant differences in baseline blood gas and acid–base values between the groups. The changes in arterial blood gases from baseline to pre-induction samples were very similar in both groups (Table 1); mean P_{aO_2} decreased by 1.34 kPa in patients who received hyoscine and by 1.07 kPa in those who received glycopyrronium, and these changes were accompanied by small reductions in haemoglobin saturation. The mean P_{aCO_2} increased by 0.73 kPa in patients who received hyoscine and by 0.63 kPa in those given glycopyrronium. These increases were statistically significant.

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Table 1. Mean (SEM) results of blood gas analysis in patients who received papaveretum with hyoscine or glycopyrronium as premedication.

	Hyoscine		Glycopyrronium	
	Baseline	Pre-induction	Baseline	Pre-induction
Pao ₂ , kPa	11.14 (0.43)	9.80 (0.32)*	11.03 (0.32)	9.96 (0.39)*
Oxygen saturation, %	95.3 (0.4)	93.2 (0.5)*	95.1 (0.3)	93.7 (0.5)*
Paco ₂ , kPa	4.66 (0.11)	5.39 (0.11)*	4.59 (0.18)	5.22 (0.18)*
pH	7.42 (0.007)	7.39 (0.005)*	7.41 (0.004)	7.40 (0.007)*
Base excess, mmol/litre	-1.11 (0.67)	0.20 (0.05)*	-2.24 (0.47)	0.13 (0.13)*

* Significant change from baseline, p < 0.05.

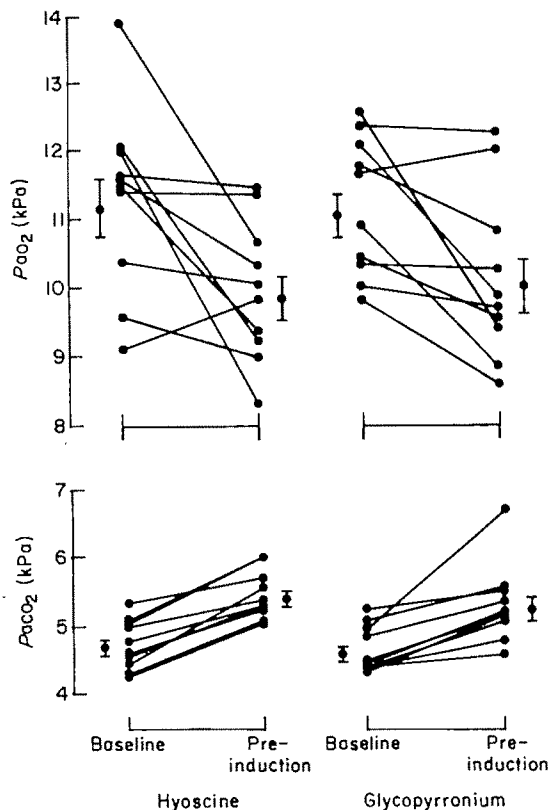


Fig. 1. Changes in Pao₂ and Paco₂ in individual patients in each group. Mean values are indicated adjacent to each set of measurements; bars represent SEM.

Individual patients from both groups had marked and clinically significant decreases in Pao₂ which were neither predictable from the baseline values nor could be explained by changes in Paco₂ (Fig. 1). The pH was slightly lower in both groups after premedication but the difference reached statistical significance in the hyoscine group only. The base excess increased slightly in both groups.

No chest pain or nausea occurred in any patient in the hour following premedication. The heart rate was 72.3 beats/minute (SEM 4.4) in the hyoscine group and 75.2 beats/minute (SEM 4.2) in the glycopyrronium group. All patients were in sinus rhythm except one in the hyoscine group who was in atrial fibrillation before premedication. The airway of one patient who received hyoscine was considered 'wet', but all others were 'dry'. Six of the 10 patients who received glycopyrronium and two of the 10 who received hyoscine were considered 'wakeful' prior to induction but this difference was not significant (Chi-squared test).

Discussion

The results of this study are similar to those reported previously following premedication with morphine and

hyoscine in patients with coronary artery disease.⁵ The combination of papaveretum and hyoscine does not appear to differ in its effect on blood gas values from morphine and hyoscine. The substitution of glycopyrronium for hyoscine did not eliminate the potential for hypoxaemia following premedication.

Changes in Pao₂ and Paco₂ in individuals in both groups were not related either to each other or to baseline values. This suggests that such changes are not due only to central respiratory depression. Anticholinergic drugs in man may cause bronchodilatation and increase physiological dead-space, an effect reported after atropine, hyoscine and glycopyrronium.^{6,7} This effect may induce a reflex increase of respiratory minute volume without change of arterial blood gases⁸ but hypoxaemia has been reported to follow administration of atropine alone.⁹ It is not known whether this effect of anticholinergics is modified by opioid drugs but hypoxaemia does not occur after morphine alone.⁵ Irrespective of the cause, the changes in mean values of blood gases and acid-base in this study may seem clinically unimportant. However, some patients suffered appreciable and unpredictable hypoxaemia, which is of special importance in patients with coronary artery disease. Pao₂ was less than 10 kPa before induction in 11 of the 20 patients; this supports the suggestion⁵ that oxygen should be administered from the time of premedication.

Acknowledgment

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References

1. PROAKIS AG, HARRIS GB. Comparative penetration of glycopyrrolate and atropine across the blood-brain and placental barriers in anesthetized dogs. *Anesthesiology* 1978; **48**: 339-44.
2. SENGUPTA A, GUPTA PK, PANDEY K. Investigation of glycopyrrolate as a premedicant drug. *British Journal of Anaesthesia* 1980; **52**: 513-6.
3. MIRAKHUR RK, DUNDEE JW, CONNOLLY JDR. Studies of drugs given before anaesthesia. XVII. Anticholinergic premedicants. *British Journal of Anaesthesia* 1979; **51**: 339-45.
4. APS C, CLEMENT AJ. Anaesthesia and cardiac disease. In: CHURCHILL-DAVIDSON HC, ed. *A practice of anaesthesia*, 5th edn. London: Lloyd-Luke, 1984: 452-516.
5. KOPMAN EA, RAMIREZ-INAWAT RC. Arterial hypoxaemia following premedication in patients with coronary artery disease. *Canadian Anaesthetists' Society Journal* 1980; **27**: 132-4.
6. SMITH TC, DUBOIS AB. The effects of scopolamine on the airways of man. *Anesthesiology* 1969; **30**: 12-18.
7. GAL TJ, SURATT PM. Atropine and glycopyrrolate effects on lung mechanics in normal man. *Anesthesia and Analgesia* 1981; **60**: 85-90.
8. NUNN JF, BERGMAN NA. The effect of atropine on pulmonary gas exchange. *British Journal of Anaesthesia* 1964; **36**: 68-73.
9. CONWAY CM, PAYNE JP. Atropine premedication and arterial oxygen tension. *Acta Anaesthesiologica Scandinavica* 1966; **10** (Suppl. 23): 538-41.

Survey of the practice of epidural analgesia in a regional sample of obstetric units

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Summary

An investigation into practices of the epidural services in a regional sample of obstetric units was undertaken following recent reported disasters associated with epidural analgesia for labour pain. A questionnaire was completed by all 22 obstetric units in the region, which included six teaching, 14 district and two independent centres. In three units the epidural service was shared with the obstetricians. A continuous anaesthetic presence was provided in 16 of 22 units. There was considerable variation in the attendance upon epidural patients by the anaesthetists. Instructions to midwives for top-ups and subsequent care of patients followed no uniform pattern. Midwife in-service training in the initial management of serious epidural complications and in cardiopulmonary resuscitation was inconsistent. In some units, the avoidance of aortocaval compression was not emphasised in the management of serious complications such as severe maternal hypotension, total spinal blockade or cardiac arrest of the parturient. The results obtained in this survey suggest that there is a need to review the requirements in the provision of obstetric epidural services and consideration should be given to the establishment of a generally accepted standard of practice.

Key words

*Anaesthetic techniques, regional; epidural.
Analgesia; obstetric.*

In recent years there have been several reports of serious maternal morbidity and mortality in association with obstetric epidural analgesia.^{1–5} An examination of present practices in obstetric epidural services was proposed in which particular attention would be paid to measures used to prevent and warn of potentially life-threatening complications.

Methods

A questionnaire† was designed to enquire into the medical responsibility and provision of the epidural service and the subsequent care of mothers in receipt of an epidural. One section enquired into details of top-up injections and subsequent patient monitoring. Information was sought about methods of recognition and treatment of complications while an epidural was in progress, as well as the relevant training and updating of midwives in areas that included cardiopulmonary resuscitation of the obstetric patient. The questionnaire included a section on the siting of first-line resuscitation equipment and drugs in relation to the mothers. There was also a section on epidural record-keeping. Finally, the extent of information afforded to patients about obstetric analgesia and, more specifically, on epidurals and possible complications, and the manner in which mothers' consent was obtained prior to the procedure, were also included in the questionnaire. An urban Regional Health Authority which offered a good cross-section of obstetric units was studied.

The investigation was started in the second half of 1985. An introductory letter which described the study and its aims was sent to the person in charge of the obstetric epidural service at each of the obstetric units of the region

under study, with the assurance that the source of information would remain confidential. This was followed by an appointment and visit by the research midwife co-authoring this study. The questionnaire was completed by the respondent in the presence of the research midwife. When the respondent was uncertain of the answer to any question that related to the practices commonly followed in that unit, the research midwife interviewed the senior registrar currently in charge of obstetric analgesia or a senior midwife from that hospital's labour ward, as appropriate, to provide the missing information. The consultant anaesthetists in charge of obstetric analgesia and anaesthesia in two teaching hospitals under study were unable to arrange a meeting with the research midwife and they completed the questionnaire by post.

Results

The region studied included six university affiliated hospitals, 14 district general hospitals and two independent hospitals. The obstetric units in one of the teaching and four of the district hospitals were isolated from the main hospital.

Size of obstetric unit and epidural rate. The number of deliveries per year was more than 4000 in one teaching and one district hospital, between 2501 and 4000 again in one teaching and one district hospital, between 1001 and 2500 in three teaching and 12 district hospitals, between 501 and 1000 in one teaching hospital and less than 501 in both independent hospitals. The epidural rate in the units surveyed ranged from less than 10% to more than 50% (Fig. 1).

Administration of obstetric epidurals. Epidurals for pain

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† The questionnaire is available from Dr M. Frank.

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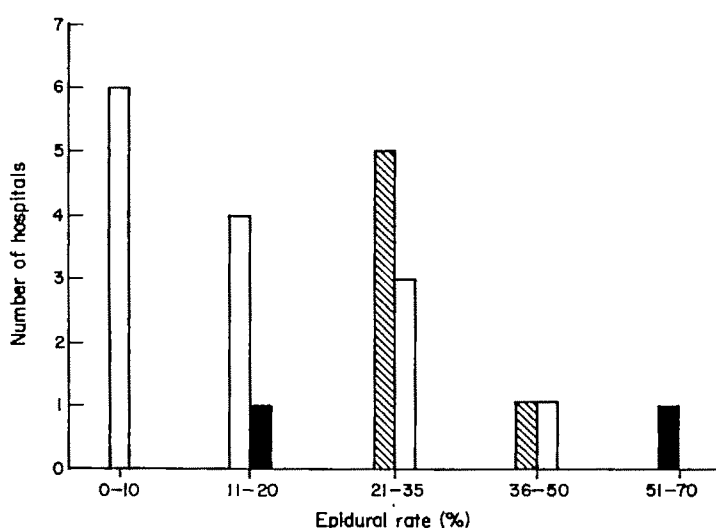


Fig. 1. Epidural rate (in 1984) in the regional sample of obstetric units surveyed. ■, Teaching; □, district; ■, independent.

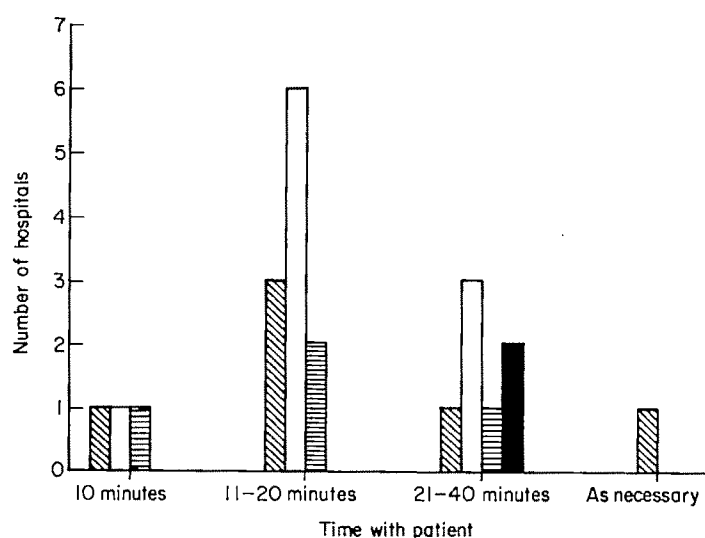


Fig. 2. Length of time anaesthetist remains with patient after first epidural injection. ■, Teaching; □, district (main hospital); ▨, district (isolated); ■, independent.

relief during labour were administered by anaesthetic staff in all teaching, 12 district and one of the independent hospitals. They were administered by an anaesthetist or an obstetrician in two district and one of the independent hospitals. Following the administration of an epidural, the time the operator remained with the patient varied from less than 10 minutes, to 40 minutes, or 'as long as necessary' in some units (Fig. 2).

The person who performed the epidural returned to see the patient frequently in two teaching, nine district (three of these isolated) and both independent hospitals, and sometimes or 'only when called' in the remaining nine hospitals.

Medical designation and availability for emergencies. There was 24-hour residential anaesthetic cover in all six teaching hospitals and in 10 of the 14 district hospitals, which included one isolated maternity unit. The designation of the first-on-call for epidural emergencies in these units was a registrar in four teaching and seven district hospitals, and an SHO or a senior registrar in the remainder, except

in one unit where an obstetrician would be the first to be called.

The anaesthetist's presence was occasional in the remaining four district hospitals (three isolated). The first-in-line in the event of an emergency was an anaesthetic registrar, SHO or, sometimes, a consultant or, in two of these units, someone from the obstetric team or from another (unspecified) medical team.

Neither independent hospital had a resident anaesthetist. In one, a consultant anaesthetist or obstetrician would be called in the event of an emergency and in the other, a consultant anaesthetist in the day time but there was no specified cover at night. The estimated time it would take to reach the epidural patient in an emergency is detailed in Table 1. The designated anaesthetist may on occasions have been unavailable for an emergency in the labour suite during day time in six hospitals and at night in 11 hospitals.

Resuscitation equipment and drugs were kept most commonly in the labour ward. In four units first-line re-

Table 1. Number of units in each hospital group where emergency would be reached within given times.

Hospital type	Time (minutes)							
	Up to 3		Up to 5		Up to 10		Up to 15	
	Day	Night	Day	Night	Day	Night	Day	Night
Teaching	4	4	1	1	1	1		
District (main)	5	3	4	5	1	2		
District (isolated)	2	1		1	2	2		
Independent			1		1	1		1

Table 2. Number of units where epidural top-ups are administered by various staff.

Hospital type	Midwife		Anaesthetist		Obstetrician	
	1st *	2nd *	1st	2nd	1st	2nd
Teaching	6	5		1	1	1
District	10	10	5	4	1	1
Independent	2		2	2	1	1

* Stage of labour.

suscitation equipment was kept in the room of the epidural mother. Resuscitation equipment and drugs were sited outside the delivery suite in three hospitals.

Epidural top-up injections. The large majority of top-ups during the first and second stages of labour were performed by midwives (Table 2). Following dural taps, the midwife continued to administer the subsequent epidural injections in three obstetric units, although this function was delegated to the anaesthetic staff in the remaining hospitals. In the three hospitals where obstetricians performed epidurals, anaesthetists were requested to do top-ups following dural taps in two, and midwives in one.

Top-up injections were preceded by a test dose in five units. The test dose varied from 10–20 mg bupivacaine, and the interval to main dose from 5–10 minutes. Top-ups were given as one injection in the remaining 17 units. Instructions on the speed of injection were specified in two of the 22 units under study. Top-up injections were preceded by test aspiration of the epidural cannula in six of the 22 hospitals. The technique of continuous infusion epidural analgesia was sometimes used in three units.

Monitoring the epidural patient and instructions to midwives. In half the teaching and independent hospitals and four of the 14 district general group, midwives were instructed to remain in the room of an obstetric epidural patient continually. They remained with the patient for 30–60 minutes following an epidural injection in the remaining units.

The mothers were wedged or on their side at all times in six units. In most of the remainder, the mothers were turned to the supine position for examination or for delivery. In three obstetric units, the mothers were wedged or turned on their side only when they showed evidence of supine hypotension.

Instructions to midwives on the recognition and treatment of an accidental subarachnoid or intravascular injection of local anaesthetic were said not to be given in two units. In 10, instructions were received as part of regular in-service training by anaesthetists, and in seven units by their midwifery tutor. In 10 hospitals, midwives received individual instructions in the labour suite, while the recognition and treatment of these complications formed part of written instructions to midwives in five obstetric units in district general hospitals.

In the event of severe maternal hypotension, midwives were instructed to increase intravenous fluids in all the hospitals surveyed. In three units they were not instructed

to tilt the patient head-down or lift the mothers' legs. In another five units the midwives were not under instruction to displace the uterus laterally as part of the treatment of severe hypotension.

Cardiopulmonary resuscitation. Training and up-dating midwives on cardiopulmonary resuscitation of the pregnant woman was said to occur regularly in six hospitals. Occasional training to midwives occurred in nine hospitals. The respondents of two district hospitals left this question unanswered and in the remaining three district and two teaching hospitals, resuscitation training to midwives was said never to be provided. The importance of the avoidance of aortocaval compression during cardiopulmonary resuscitation was said on direct questioning 'to be stressed' in 14 units.

Treatment by medical staff of severe complications. In the event of total spinal blockade, the medical staff in all hospitals would increase intravenous fluids, provide oxygenation and intubate the trachea if indicated. The treatment offered in five hospitals did not include head-down tilt or raising the patients' legs, and in three units did not include ephedrine. The avoidance of aortocaval compression was not part of the treatment of a total spinal block in three hospitals.

Epidural records. Epidural records were kept in all but one independent hospital. These were reviewed regularly in five of the six teaching, and half of the district units. In two district and one independent hospital they were never reviewed. They were reviewed occasionally in the remaining units that kept records.

Patient information and consent. Possible complications of epidural analgesia were described fully in one of the 22 units under study; this was one of the independent hospitals. In 15 units, complications were partly described and in five, they were mentioned only when asked by the mother. In one unit, the possible complications of epidural analgesia were said not to be discussed with the mothers. Their written consent was obtained in nine units and verbal consent in 12. In one district hospital the mothers' consent was not asked for prior to administration of an epidural.

Accidental spinals or toxic reactions. The actual number of accidental spinal blocks or occurrence of convulsions in epidural obstetric patients over the preceding 12 months (1984–85) was enquired into. Three patients received accidental subarachnoid injections but there were no reports of convulsions following epidural analgesia for labour pain. All mothers were treated successfully.

Discussion

A study of birth facilities revealed that epidural analgesia was given to 120 000 mothers out of 705 000 deliveries in England and Wales in 1983.⁶ At Queen Charlotte's Hospital, there have been approximately 30 000 epidurals over the last 15 years, during which time the only major problems consisted of three total spinals which were all treated successfully (B.M. Morgan, personal communication). In a review by Crawford⁷ of 27 000 epidurals for analgesia in labour, nine potentially life-threatening complications are described from which complete recovery was made in all cases. In a nationwide survey of obstetric units in Sweden, there were 84 188 vaginal deliveries in 1982 and 11 324 epidurals performed for labour pain relief; there were no reports of permanent neurological damage or maternal deaths.⁸ In the present survey, it was estimated that 44 000 deliveries took place in the year studied and 10 000 epidurals were administered; a total spinal was reported on three occasions, with no permanent sequelae.

In the *Reports on Confidential Enquiries into Maternal Deaths in England and Wales*,^{1,2} two deaths were reported in 1973–75 and one death in 1976–78 as a consequence of epidural analgesia for relief of pain in labour. In 1984 one maternal death and one case of irreversible brain damage followed epidural injections for obstetric analgesia.⁴ The nature of the disasters described indicates clearly that a medically designated person fully skilled in resuscitation of an obstetric patient should be readily available and that resuscitation equipment and drugs should be in the immediate vicinity.^{9,10}

Since 1971, it has been officially accepted practice for the midwife to administer epidural top-ups and to monitor the mother.¹¹ The midwife is therefore expected to be aware of methods of prevention of related complications and their immediate recognition and initial treatment should they arise. Increased or special risks during top-up administrations are present if subsequent epidural injections are given following an initial dural tap, or during the second stage of labour. In the latter example there are concomitant maternal postural changes, the midwife's attention is naturally diverted towards the conduct of the delivery and a degree of urgency may be imposed upon the top-up. One woman who had sustained a recognised dural tap during the epidural insertion, died of a total spinal following a top-up injection by a midwife.¹ Two recent disasters occurred following top-ups by midwives during the second stage.⁴ In the region under study, three units delegated midwives to give subsequent epidural top-up injections after an initial dural puncture and in 15 hospitals midwives gave top-ups during the second stage.

In the majority of units the top-ups were given as a single injection and were not preceded by test aspiration of the cannula, nor was speed of injection specified. There has been much argument about the value of these safety precautions, in particular the use of test doses prior to all epidural injections.^{9,10,12–15} A more recent development is the continuous infusion epidural which offers several potential advantages.^{16–18} This technique has had limited use to date.

Serious reactions have been reported some time after the epidural injection; in particular, Thorburn and Moir¹⁹ described two patients (albeit for Caesarean section) who developed grand mal convulsions 20 minutes later. Total spinal analgesia following a subdural injection may be slow to develop^{20–22} and the need for the continuous presence of the midwife with an epidural patient should be considered. The midwives remained with the mothers throughout in eight of the 22 units surveyed and they were required to stay with the epidural patients for at least 30 minutes after each top-up in the remaining hospitals.

If complications occur it is the midwife who is on the spot and therefore should be trained in the immediate recognition of possible complications and be able to initiate the correct treatment and manage the situation until the anaesthetist arrives. To this end, in-service education of midwives must be pertinent and well organised. Our findings show a failure of this process in many units.

In the present survey, the most commonly overlooked single factor during treatment of severe maternal hypotension or the institution of resuscitative measures, was aortocaval compression. Uterine displacement would not be part of the proposed management of maternal hypotension in five centres and the importance of avoidance of aortocaval occlusion was not stressed in the teaching of obstetric cardiopulmonary resuscitation in eight hospitals. The hazards of the supine position in late pregnancy have been reported extensively.^{10,23,24} Marx and Bassell,²³ in their review of this problem, concluded: 'Attempts to raise maternal blood pressure with intravenous hydration will be doomed to failure unless adequate displacement of the uterus from the inferior vena cava has first been assured. Likewise, in the rare situation in which cardiac resuscitation becomes necessary, the gravid uterus must not be allowed to interfere with cardiac filling.'

In conclusion, the results from this study show great diversity in the standards of care afforded to obstetric patients who receive epidural analgesia in an urban Regional Health Authority. It is likely that this survey reflects practices in other regions and it is suggested that there is a need to review and standardise obstetric epidural services in an attempt to maximise the safety of this established and useful form of analgesia.

Acknowledgments

We thank Drs B. Morgan and D. Moir for their assistance and helpful suggestions. This project was supported with a research grant from Astra Pharmaceuticals Ltd.

References

1. TOMKINSON J, TURNBULL A, ROBSON G, CLOAKE E, ADELSTEIN AM, WEATHERALL J. *Report on confidential enquiries into maternal deaths in England and Wales 1973–75*. London: HMSO, 1979.
2. TOMKINSON J, TURNBULL A, ROBSON G, DAWSON I, CLOAKE E, ADELSTEIN AM, ASHLEY JE. *Report on confidential enquiries into maternal deaths in England and Wales 1976–79*. London: HMSO, 1982.
3. CORKE BC, SPIELMAN FJ. Problems associated with epidural anaesthesia in obstetrics. *Obstetrics and Gynecology* 1985; **65**: 837–9.
4. WINN D. How dangerous is the birth jab? *Sunday Times* 1984 Aug 26.
5. BRAHAMS D. Record award for personal injuries sustained as a result of negligent administration of epidural anaesthetic. *Lancet* 1982; **1**: 159.
6. MORGAN BM. Confidential enquiry into facilities available at place of birth (in press).
7. CRAWFORD JS. Some maternal complications of epidural analgesia for labour. *Anaesthesia* 1985; **40**: 1219–25.
8. HANSON B, MATOUSKOVA-HANSON A. Continuous epidural analgesia for vaginal delivery in Sweden. Report of a nationwide inquiry. *Acta Anaesthesiologica Scandinavica* 1985; **29**: 712–5.
9. CRAWFORD JS. *Principles and practice of obstetric anaesthesia*, 5th edn. Oxford: Blackwell Scientific Publications, 1984.
10. MOIR DD. Local anaesthetic techniques in obstetrics. *British Journal of Anaesthesia* 1986; **58**: 747–59.
11. TOWLER J, BUTLER-MANUEL R. *Modern obstetrics for student midwives*, 2nd edn. London: Lloyd-Luke Ltd, 1980.
12. MARX GF. Cardiotoxicity of local anesthetics—the plot thickens. *Anesthesiology* 1984; **60**: 3–5.

13. MOORE DC, BATRA MS. Concerning the use and abuse of test doses for epidural anesthesia. *Anesthesiology* 1984; **61**: 345-6.
14. PRINCE G, MCGREGOR D. Obstetric epidural test doses. A reappraisal. *Anaesthesia* 1986; **41**: 1240-50.
15. CRAWFORD JS. Test doses for epidural analgesia—are we fooling ourselves? *Anaesthesia* 1986; **41**: 766.
16. MATOUSKOVA A, HANSON B, ELMEN H. Continuous mini-infusion of bupivacaine into the epidural space during labor. Part III. A clinical study of 225 parturients. *Acta Obstetrica et Gynaecologica Scandinavica* 1979; **83** (Suppl.): 43-52.
17. MORISON DH, SMEDSTAD KG. Continuous infusion epidurals for obstetric analgesia. *Canadian Anaesthetists' Society Journal* 1985; **32**: 101-4.
18. EWEN A, MCLEOD DD, MACLEOD DM, CAMPBELL A, TUNSTALL ME. Continuous infusion epidural analgesia in obstetrics. A comparison of 0.08% and 0.25% bupivacaine. *Anaesthesia* 1986; **41**: 143-7.
19. THORBURN J, MOIR DD. Bupivacaine toxicity in association with extradural analgesia for Caesarean section. *British Journal of Anaesthesia* 1984; **56**: 551-3.
20. CONKLIN KA, VAN DER WAL C. Epidural anaesthesia with chloroprocaine. Delayed onset, extensive spread, and prolonged duration. *Anaesthesia* 1980; **35**: 202-4.
21. COLLIER C. Total spinal or massive subdural block? *Anaesthesia and Intensive Care* 1982; **10**: 92.
22. LEE A, DODD KW. Accidental subdural catheterisation. *Anaesthesia* 1986; **41**: 847-9.
23. MARX GF, BASSELL GM. Hazards of the supine position in pregnancy. In: ROSEN M, ed. *Clinics in obstetrics and gynaecology, obstetric anesthesia and analgesia*. London: W.B. Saunders, 1982.
24. BROMAGE PR. *Epidural analgesia*. Philadelphia: W.B. Saunders, 1978.

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General anaesthesia in minor surgery and myocardial infarction

The associated risk of the combination of acute myocardial infarction, noncardiac surgery and general anaesthesia is well known, as is the crucial importance of the interval of time between infarction and surgery.^{1–4} Surgery is therefore postponed, if possible for at least 6 months after acute myocardial infarction. This generally includes even minor surgery, although the lethal relationship is conceivably much less. This attitude may also in part be because we know even less about the influence of anaesthesia *per se* on the course of ischaemic heart disease. Prospective controlled trials would not for obvious reasons be ethically acceptable.

However, 26 patients with recent myocardial infarction had a permanent pacemaker implanted in our department during 1978–84; 16 of these received general anaesthesia, the rest regional anaesthesia. This procedure has since 1984 been performed entirely with regional anaesthesia. Assuming the surgical procedure of pacemaker implantation to be very minor, we decided to examine peri-operative and post-operative morbidity in these two groups. The New York Heart Association's classification of the patients and other details are given in Table 1.

All patients except one, had temporary cardiac electrodes

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Table 1. Patient data and NYHA classification.

	Local anaesthesia (n = 10)	General anaesthesia (n = 16)
Sex, M:F	6:4	12:4
Mean age, years (range)	70 (56-88)	69 (41-86)
NYHA group I	2	2
NYHA group II	5	6
NYHA group III	2	3
NYHA group IV	1	5
Infarction \leq 3 weeks	6 (60%)	7 (44%)
Infarction \leq 3 months	3 (30%)	7 (44%)
Infarction \leq 6 months	1 (10%)	2 (12%)

inserted before the pacemaker was implanted. The anaesthetic technique in 11 patients was thiopentone induction and halothane, nitrous oxide and oxygen inhalation; in five patients, thiopentone, pethidine, nitrous oxide and oxygen. Tracheal intubation was necessary in two patients. The median duration of anaesthesia was 90 minutes (range 45-420 minutes) and two patients had hypotension during anaesthesia: profound hypotension lasted a few minutes in one patient and in the other, moderate hypotension persisted during the whole procedure. Both these patients were in NYHA group IV and had episodes of pulmonary oedema before anaesthesia. They both died, respectively 4 and 13 days after anaesthesia. Local anaesthesia was with lignocaine 2% plain solution and one patient died 3 days after the procedure. He also was in NYHA group IV and had episodes of pulmonary oedema before surgery.

No patient had reinfarction diagnosed during the first 3 weeks after surgery. No difference in postoperative mortality

was found after general or regional anaesthesia for a minor surgical procedure performed in patients with recent myocardial infarction. The use of general anaesthesia in minor surgery may be less hazardous than generally thought in patients with recent myocardial infarction, excluding those with overt heart failure who are at high risk whatever is done.

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References

1. GOLDMAN L, CALDERA DL, SOUTHWICK FS, NUSSBAUM SR, MURRAY B, O'MALLEY TA, SOROLL AH, CAPLAN CH, NOLAN J, BURKE DS, KROGSTAD D, CARABELLO B, SLATER EE. Cardiac risk factors and complications in non-cardiac surgery. *Medicine* 1978; **57**: 357-70.
2. RAO TLK, EL-ETR AA. Myocardial reinfarction following anesthesia in patients with recent infarction. *Anesthesia and Analgesia* 1981; **60**: 271-2.
3. STEEN PA, TINKER JH, TARHAN S. Myocardial reinfarction after anesthesia and surgery. *Journal of the American Medical Association* 1978; **239**: 2566-70.
4. TARHAN S, MOFFITT EA, TAYLOR WF, GIULIANI ER. Myocardial infarction after general anesthesia. *Journal of the American Medical Association* 1972; **220**: 1451-4.

Postoperative laryngospasm triggered by acute angina?

Postoperative laryngeal spasm is often due to an irritative stimulus to the airway during recovery from general anaesthesia; less commonly, it may arise as a result of noxious visceral or somatic stimuli. We report an unusual case of the latter.

A 60-year-old farmer with a history of frequent angina precipitated by moderate exertion and anxiety, was admitted for repair of right inguinal hernia and hydrocele. He had needed coronary care 18 months previously for severe central chest pain which radiated to his left arm; an electrocardiogram then showed ischaemic changes in the inferior leads (downward sloping ST segment and inverted T-wave in leads III and aVF). Serial aspartate transaminase levels were normal and he was started on atenolol 50 mg and nitroglycerine spray. Nifedipine retard 20 mg was added when chest pain recurred the following night and he was discharged in stable condition one day later.

Exertional and resting angina relieved by GTN, were noted pre-operatively to recur despite medical therapy. Clinical examination was normal; the ECG showed mild ST elevation and T-wave inversion in lead III, and blood investigations and chest X ray were relatively normal. Epidural or spinal analgesia was offered but the patient was reluctant to accept either method, so general anaesthesia was chosen.

Cyclimorph 10 mg was given intramuscularly as pre-medication one hour before operation; a 5-mg Transiderm-Nitro patch was applied, inadvertently only 20 minutes before operation. Induction with thiopentone 300 mg intravenously was followed by 7 mg vecuronium for tracheal intubation and controlled ventilation of the lungs with nitrous oxide, oxygen and enflurane. Operation and anaes-

thesia lasted 30 minutes and were uneventful. Reversal of relaxant drugs, tracheal extubation and recovery were uncomplicated; the patient responded verbally to questions and breathed low flows of oxygen from a Hudson facemask. Severe upper airway stridor occurred 6 minutes later with respiratory distress. Oxygen flow was increased; on inspection his throat was clear of secretions. Intravenous doxapram¹ 30 mg in total gave no relief from laryngeal spasm and he became increasingly restless. Papaveretum was then given in increments intravenously for sedation; a dose of 10 mg alleviated his laryngeal spasm but it recurred intermittently. The patient was much less distressed after a further 5 mg but stated that it was his angina that was troubling him all along. His chest pain disappeared completely and he was breathing comfortably within 2 minutes of applying GTN spray sublingually. Hypotension and bradycardia ensued 30 minutes later and were corrected with intravenous atropine 0.3 mg. Vital signs remained stable afterwards; no new features appeared on a post-operative ECG and the patient went home 3 days later.

We suggest that this man's postoperative laryngospasm was triggered by a paroxysm of angina, abetted by acute anxiety and postoperative pain. Anti-anginal protection by the nitroglycerine patch was probably insufficient in view of its late pre-operative application. Oxygenation was ensured in this case but doxapram failed to relieve his laryngeal spasm; papaveretum was more successful and allowed the patient to indicate that the main problem was his angina.

Posterior and inferior myocardial ischaemia has been associated with various parasympathetic effects. A high incidence of hypotension, bradycardia, sialorrhoea, nausea,

bronchospasm and tracheal burning has been noted in patients with acute posterior and inferior myocardial infarction as a vagal reflex from ischaemic stimulation of atrial cholinergic ganglia and nerve endings.² Bradycardia and hypotension may occur during vasotonic angina pectoris, similar to a Bezold Jarisch reflex.³ Vagal afferents from the larynx, trachea and lungs are known to elicit laryngeal reflexes.⁴ It is possible that cardiac vagal afferents may behave similarly when activated by myocardial ischaemia but, as yet, no direct clinical or experimental evidence has been obtained from previous literature.

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Hypersensitive carotid sinus

The paper by Dr I. McConachie (*Anaesthesia* 1987; 42: 636-8) was interesting. We wish to report the following case of a patient who developed syncopal attack due to inadvertent carotid sinus compression before the start of general anaesthesia. He was subsequently found to have a hypersensitive carotid sinus.

A 72-year-old male presented for right extracapsular lens extraction and intra-ocular lens implantation. He had no symptoms of intercurrent cardiac or respiratory disease. The patient had diabetes which was well controlled with 5 mg glibenclamide daily. He had received three uneventful general anaesthetics prior to this admission, one for extracapsular lens extraction in the left eye. The only significant finding in the pre-operative ECG was the presence of left anterior hemiblock. Similar findings were present in the ECG taken 4 years ago. All other biochemical and haematological investigations were within normal limits. He received pethidine 25 mg, promethazine hydrochloride 25 mg and atropine 0.6 mg intramuscularly as premedication. The same drugs were used as premedication on the previous two occasions. The patient was sleepy but rousable. 45 minutes later. His pulse rate was 72 beats/minute and arterial blood pressure 130/70 mmHg. He was wheeled on a stretcher to the operating theatre and transferred to the operating table. The operating room attendant tried to help the patient to raise his head by holding his occiput and neck in order to change the pillow.

The patient complained that he felt dizzy and began to sweat profusely within a minute of this manoeuvre. His pulse rate was 45 beats/minute and blood pressure 90/60 mmHg. The pulse rate decreased to 16 beats/minute over the next minute and the ECG monitor which was connected at this time showed sinus bradycardia. The patient was given oxygen by mask and the heart rate increased gradually to 60 beats/minute. The patient was conscious and well aware of his surroundings throughout this episode. He was transferred to the intensive care unit with a provisional diagnosis of acute myocardial injury. Hypoglycaemia and drug allergy were excluded. His stay in the intensive care unit was uneventful. The patient was evaluated by a cardiologist and it was found that application of mild carotid sinus compression resulted in severe bradycardia of 12

References

1. OWEN H. Postextubation laryngospasm abolished by doxapram. *Anaesthesia* 1982; 37: 1112-4.
2. SCHLANT RC. Altered cardiovascular physiology of coronary atherosclerotic heart disease. In: HURST JW, LOGUE RB, SCHLANT RC, WANGER NK, eds. *The heart, arteries and veins*. New York: McGraw Hill, 1978: 1134-56.
3. ROBERTSON D, BERNARD Y, ROBERTSON RM. Cardiogenic reflexes associated with spontaneous coronary spasm in patients with vasotonic angina pectoris (Abstract). *Circulation* 1980; 62: III-312.
4. REX MAE. A review of the structural and functional basis of laryngospasm and a discussion of the nerve pathways involved in the reflex and its clinical significance in man and animals. *British Journal of Anaesthesia* 1970; 42: 891-9.

beats/minute. It was therefore thought that the patient might have had inadvertent carotid sinus compression during the pillow change which resulted in severe bradycardia and a syncopal attack.

This emphasises the need to identify patients beforehand who have a hypersensitive carotid sinus. Severe bradycardia and circulatory insufficiency could result from inadvertent carotid sinus compression during head and neck manipulations.

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A reply

Thank you for allowing me the chance to comment on the above letter. My review was concerned primarily with carotid sinus massage in patients with sick sinus syndrome but the authors are correct to point out that patients with hypersensitive carotid sinuses can also be identified before operation by carotid sinus massage (even if only accidentally, as in this case). There is controversy whether sick sinus syndrome and carotid sinus hypersensitivity are related disorders which may occur simultaneously in some patients¹ but intra-operative complications can also be dangerous in patients with carotid sinus hypersensitivity.² I therefore thank the authors for supporting my view that identification of such patients by carotid sinus massage is important.

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References

1. COPLAN NL, SCHWEITZER P. Carotid sinus hypersensitivity. Case report and review of the literature. *American Journal of Medicine* 1984; 77: 561-5.
2. BROWN CQ, WATSON CB. Carotid sinus syndrome: intra-operative management facilitated by temporary transvenous demand pacing. *Anesthesiology* 1982; 56: 151-3.

Consultants and pre-operative visits

This writer wholeheartedly supports Dr Bethune's plea for the leaders of our profession to stress the importance of the pre-operative visit (*Anaesthesia* 1986; 42: 553-4). One way in which this could be done is by Faculty Visitors but, in our experience in the Mersey Region, there is consider-

able variation in how much importance such Visitors attach to this aspect of training of our junior staff.

It is unfortunate that Curran and colleagues¹ seem to suggest that the personal pre-operative visit by an anaesthetist is time consuming and inefficient, and that an equally

good method is a telephone call from house surgeon to anaesthetist. Do these authors really consider that the training and experience of an anaesthetist are equivalent to those of a house surgeon in assessing the anaesthetic implications of the patient's history, examination and investigations? Does personal contact between patient and anaesthetist contribute nothing to the care of the patient?

Anaesthetists have contributed by their failure to visit patients pre-operatively, to the view of other doctors that anaesthetists are largely technicians; our medical and surgical colleagues will not recognise that anaesthetists have clinical skills until these skills are seen in action on the wards. It is also true that many members of the general public still regard anaesthetists as non-doctor technicians. They will continue to fail to recognise us as doctors until they hear more often on the ward, 'I am doctor X, your anaesthetist' and then meet that same doctor in the anaesthetic room.

All new consultant contracts include sessions for pre-

operative and postoperative care. A session, in the sense of three and a half consecutive hours for pre-operative assessment, is obviously inapplicable to an anaesthetist's pattern of work but consultants with such sessions should be seen to give an appropriate amount of time to personal pre-operative assessment. It would be a seriously retrograde step to return to the days when the anaesthetist spent so much time in the operating theatre that there really was no time to see patients on the ward.

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M.E. DODSON

Reference

1. CURRAN J, CHSMIELSKI AT, WHITE JB, JENNINGS AM. Practice of pre-operative assessment by anaesthetists. *British Medical Journal* 1985; 2: 391-3.

Minimal monitoring

One agrees fully with the desirability and cost effectiveness of routinely using an oxygen analyser on the inspiratory limb of the patient breathing system and of using a ventilation monitor (Editorial, *Anaesthesia* 1987; 42: 683-4) but I consider that the use of a continuous monitor of the circulation should also be strongly encouraged. An ECG on its own, whilst it provides useful information, does not release the anaesthetist from the task of continuously monitoring the circulation. A finger on the pulse, ideally combined with precordial or oesophageal stethoscopy, may suffice for brief uncomplicated cases. A digital pulse meter (plethysmograph) provides an indicator of circulatory adequacy at very reasonable cost, may also be used to facilitate regular systolic blood pressure measurements when access to the patient is difficult, and signals the occurrence of dysrhythmias. These

devices may be used in induction rooms, during patient transport and in the field, and should be affordable in areas where the availability of an ECG machine for every operating theatre is considered too expensive. Pulse oximetry is yet more desirable but its introduction has been delayed by cost constraints. Thus, whilst the ECG does provide additional information about cardiac rhythm and myocardial ischaemia it only complements but does not replace some other continuous monitor of circulatory adequacy.

Flinders Medical Centre,
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W.B. RUNCIMAN

One year's experience with the APACHE II system in a general intensive care unit

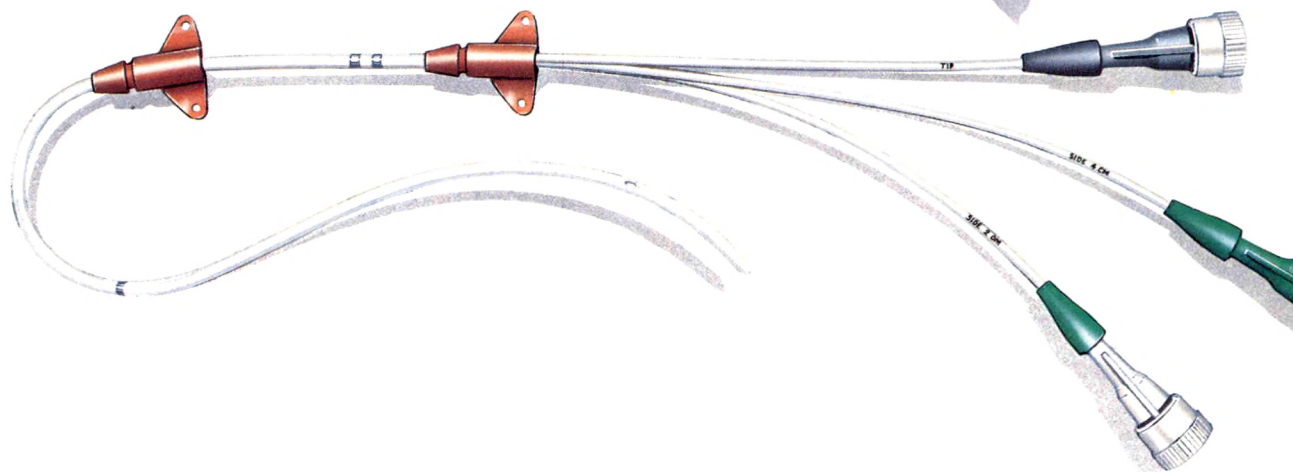
We would like to comment on the article (*Anaesthesia* 1987; 42: 738-44) by Dr Jacobs and colleagues about their use of the APACHE II scoring system¹ to predict outcome in critically ill patients. They derived separate Risk of Death values on day 1 and day 3 of ICU stay in 58 patients; patients were then predicted to die if they had either a Risk of Death of 60% or more on day 1, or a Risk of Death less than 60% on day 1 but more than 30% on day 3. This classification correctly predicted death in seven of 24 patients who died (a sensitivity of 29%), and correctly predicted survival in all 34 survivors (a specificity of 100%). This underestimation of Risk of Death at high levels of risk is also reflected in their predictions of outcome based on day 1 data, as shown in the lower part of Table 6. While the overall performance is appropriate if APACHE scoring is to be used for withdrawal of treatment, as an index of severity of illness, considered simply as a system of measurement, it is inaccurate at these higher levels.

We have also examined² the use of change in severity scores (SS) over time in 128 critically ill patients, 71 of whom were still in the ICU by day 4. Instead of looking only at those patients whose Risk of Death was less than 60% on day 1 and more than 30% on day 3, we examined the effect of change in severity scores for all patients at all levels of initial severity of illness. Patients were categorised

into bands of increasing severity of illness on admission; the change in a patient's SS (by day 4, for example) was measured as a ratio of (SS on day 4 - SS on admission) to SS on admission. Using logistic regression and a risk level of 50% we obtained an overall correct classification rate of 80%, with a sensitivity of 75% and a specificity of 87%. In addition, we showed that survival from the most severe levels of illness is associated with a decrease in mean (SEM) SS of 45% (5.1) by day 4, while non-survivors improved by only 18% (5.28). At intermediate levels of severity, survivors improved by 22% (6.5), while non-survivors showed a mean increase in illness severity of 3.8% (7.43) by day 4.

The capacity of the APACHE II score to predict outcome is an index of its accuracy as a measure of severity of illness, and it is important that we remember this: it is a ruler, not a crystal ball. It should be used as a guide to clinical judgment, not as a substitute for it, and Dr Jacobs' caveats are entirely appropriate. For this reason it is important that severity scoring should be examined over time and not as a single assessment at the time of admission. This approach has a number of advantages. It enables staff to identify a global improvement or deterioration in a patient's clinical condition; it directs attention to patients whose care could be improved; and it may be possible by incorporating an index of change in SS, to develop scoring systems which do

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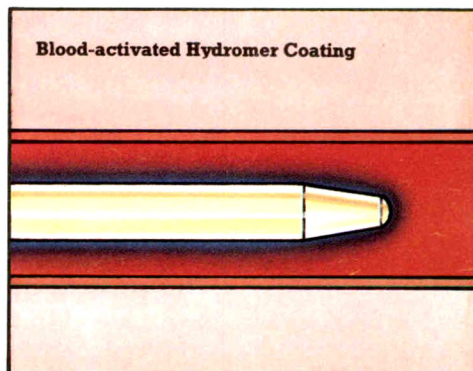
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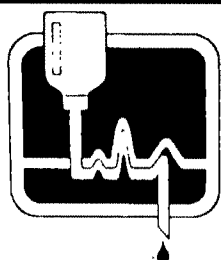
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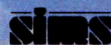
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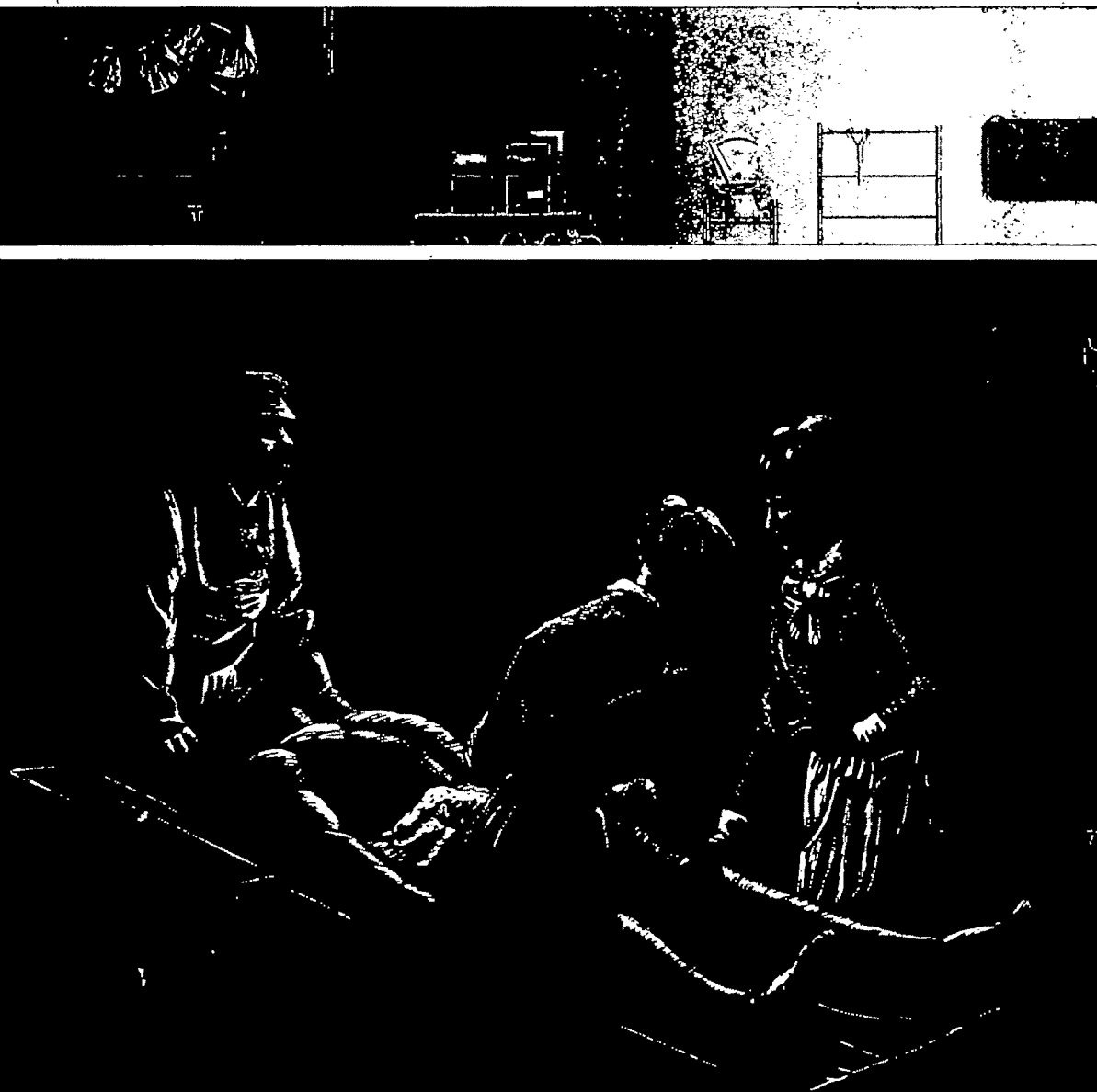
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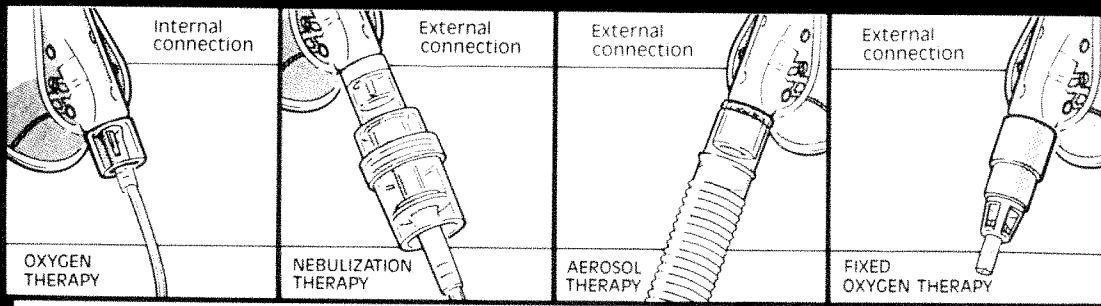
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J. BION
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References

1. KNAUS WA, DRAPER EA, WAGNER DP, ZIMMERMAN JE. APACHE II: a severity of disease classification system. *Critical Care Medicine* 1985; 13: 818-29.
2. BION JF, AITCHISON TC, EDLIN SA, LEDINGHAM IMCA. Sickness scoring and response to treatment as predictors of outcome from critical illness. *Intensive Care Medicine* (in press).

A reply

We are grateful for an opportunity to comment on this letter. We agree that the best approach to reflect the dynamic pathophysiological changes that occur in our critically ill patients is by APACHE II assessments over time.

Unfortunately, Dr Bion and colleagues are somewhat confused in the reading of the data presented in Table 8. The second column and last row of Table 8 gives the total number of patients predicted to die, which was 7, and all seven died (specificity of prediction of death, 100%). The first column, last row gives the total number predicted to live (51), out of whom 34 lived and 17 died. The formulae used to calculate specificity and sensitivity of predictions of death are as follows:

$$\begin{aligned}\text{specificity (\%)} &= \frac{\text{PredDDead}}{\text{PredDDead} + \text{PredADeal}} \times 100 \\ \text{sensitivity (\%)} &= \frac{\text{PredAAlive}}{\text{PredAAlive} + \text{PredDALive}} \times 100\end{aligned}$$

where PredDDead is the number predicted to die, who died; PredDALive is the number predicted to die, who lived; PredAAlive is the number predicted to live, who lived; and PredADeal is the number predicted to live, who died.

There does appear to be an underestimation of the Risk of Death at high levels of risk (Table 6). This is especially the case when our data are compared with those published by Knaus.¹ We have put forward several possible explanations² for this. Our patient mix is quite different from that reported by Knaus, with more patients with end-stage chronic disease, and we use the best Glasgow coma score for the 24-hour period and not the worst, as described by Knaus. This gives us lower APACHE scores and therefore Risk of Death. We use the best Glasgow coma score in

order to give our patients the benefit of the doubt and also because it appears to improve the specificity of our predictions.

Since our paper was submitted, we have performed daily APACHE II assessments to reflect the *dynamic* pathophysiological changes that occur in ICU patients, and to eliminate further the element of chance inherent in a two-assessment model. We have been able to develop predictive criteria to predict death among ICU patients using trend analysis of the daily APACHE II scores. The analysis takes into account the absolute value of the APACHE II score on each day and the rate of change relative to that of the previous day. We found that with over 600 patients there was no patient who survived with an APACHE II score greater than 35. There was a 'fuzzy zone' for patients admitted with scores between 30 and 35; these patients died unless they improved their day 2 score by >3. In patients admitted with reasonable APACHE II scores who subsequently deteriorated, those who suffered an increase in the APACHE score of >2 relative to that of the previous day, and with an absolute score exceeding 27, all died. One hundred consecutive adult ICU admissions were used to determine these criteria. They were then tested on a further 112 consecutive adult ICU admissions. Our model predicted correctly 16 out of the 34 patients who died. None of the predictions was used to influence clinical decision making.

We still perform day 1 Risk of Death but no longer use daily Risk of Death because its derivation is based on subjective choice of a single specific diagnostic category or major organ system as the primary cause for admission to the ICU. The correct choice can sometimes be extremely difficult to make. This is especially the case among patients with multi-organ system failure. It is also common for ICU patients to develop other major organ system failures during their stay in the ICU. The choice of a single specific diagnostic category does not reflect this important aspect of the progress of an ICU patient. Lastly, the specific diagnostic coefficients were developed from day 1 data and therefore may not be applicable for subsequent days.

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References

1. KNAUS WA, DRAPER EA, WAGNER DP, ZIMMERMAN JE. APACHE II: a severity of disease classification system. *Critical Care Medicine* 1985; 13: 818-29.
2. CHANG RWS, JACOBS S, LEE B, PACE N. Predicting deaths among ICU patients. *Critical Care Medicine* (in press).

Premedication and postoperative vomiting

The paper by Drs Cross and Barrett (*Anaesthesia* 1987; 47: 845-9) was very interesting and I am sure that regional block analgesia should be regarded as the standard for this type of procedure, and anything else a second best. Nevertheless, the high level of postoperative vomiting was distressing to me (and probably to the patients), and the way in which it seems to be viewed as an inevitable consequence of anaesthesia. A passing reference to opioid premedication suggests that a thoroughly well-established fact is still not appreciated: opioid premedication results in a high incidence of vomiting and contributes little or nothing to the overall anaesthetic.¹ Many children describe the injection on the

ward as the worse part of their stay in hospital.^{2,3} Is this a good start to their anaesthetic?

The art of anaesthesia has, I hope, advanced since 1911 when Buxton described the use of morphine and atropine premedication to the anaesthetic section of the Royal Society of Medicine but, as Inglis and Barrow⁴ pointed out in 1965, 'Tranquillization extended over days can help everyone, but just to inject the patient one hour pre-operatively in order to render him drowsy, confused, dizzy, and perhaps nauseated, is a thoughtless shirking of responsibility.' I sometimes wonder.

Perhaps our patients would appreciate us more if we were

not such a conservative lot. Beecher⁵ pointed out almost 30 years ago: 'Empirical procedures firmly entrenched in the habits of good doctors seem to have a vigour and life, not to say immortality, of their own.'

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D.H. CHAPMAN

References

1. BOOKER PD, CHAPMAN DH. Premedication in children undergoing day-care surgery. *British Journal of Anaesthesia* 1979; **51**: 1083-7.
2. DOUGHTY AG. The evaluation of premedication in children. *Proceedings of the Royal Society of Medicine* 1959; **52**: 823-34.
3. BOYD JD, MANFORD MLM. Premedication in children. A controlled clinical trial of oral Triclops and diazepam. *British Journal of Anaesthesia* 1973; **45**: 501-6.
4. MCNAUGHT INGLIS J, BARROW MEH. Premedication: a reassessment. *Proceedings of the Royal Society of Medicine* 1965; **58**: 29-32.

5. BEECHER HC. *Measurement of subjective responses: quantitative effects of drugs*. New York: Oxford University Press, 1959.

A reply

Thank you for the opportunity to reply. We pointed out in our paper that there are additional factors and influences apart from premedicant drugs that confuse the aetiology of the single vomit in the postoperative period (often associated with the first intake of oral fluids). Dr Chapman's comments are noted but the intention of the investigation was to compare two methods of regional analgesia as a supplement to general anaesthesia; the choice of premedication in children continues to be a controversial issue and no particular method, route of administration or choice of agent(s) has been found to be ideal and without complication.

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G.D. CROSS
R.F. BARRETT

Unstable cervical fracture

We read with interest the case report by Dr J.R. Eason and colleagues (*Anaesthesia* 1987; **42**: 745-9) about the anaesthetic management of an unstable cervical fracture. This is always a delicate problem and is made more difficult in the patient with a full stomach. Any manipulation of the neck risks damage to the spinal cord and must be avoided at all costs. We have faced this situation twice in recent weeks and chose to intubate both patients using a fiberoptic bronchoscope.

Our first patient was a 29-year-old man who had been involved in a motor cycle accident. He had sustained fractures to his left femur, both lower legs, the 10th-12th ribs on the right side and a fracture through the base of the odontoid peg. He had eaten just prior to his accident. He required transfusion of six units of blood and 1000 ml polygeline to maintain his blood pressure. Peritoneal lavage returned heavily blood-stained fluid and he was scheduled for an urgent laparotomy. He was transferred to the operating room; after our intentions were explained to the patient topical anaesthesia was achieved with 4% lignocaine gargle and transtracheal injection without production of coughing. We then passed the fiberoptic bronchoscope with a well-lubricated size 8.0 plastic tracheal tube mounted on it, through the mouth and into the trachea until the tip was just above the carina. The tracheal tube was then advanced gently into the trachea. Anaesthesia was induced with fentanyl, thiopentone and vecuronium immediately the tube was positioned and the cuff inflated. Postoperatively the patient had no neurological deficit.

Our second patient was a 53-year-old man injured by a falling bale of cotton, in whom X rays showed a fracture of the third cervical vertebra. The patient had a depressed level of consciousness and appeared to be quadriplegic; blood gas analysis revealed marked respiratory acidosis. A fiberoptic bronchoscope with a size 7.5 plastic tracheal tube mounted on it was passed without anaesthesia through the nose and into the trachea until the tip was just above the carina. The tracheal tube was then advanced into the trachea and ventilation commenced. There was a marked improvement in the patient's conscious level once the hypercapnia was corrected but he remained quadriplegic.

The use of the fiberoptic bronchoscope for the intubation of patients with cervical spine fractures allows intubation to be performed without manipulation of the patient's neck and seems to be the method of choice in these patients. Dr

Eason and colleagues state in their article that 'fiberoptic intubation by the nasal route is more difficult in the supine position'; this may be so in an anaesthetised supine patient if the tongue is allowed to fall back onto the posterior pharyngeal wall. We do not find bronchoscopic intubation in supine patients difficult, whether it be by the oral or nasal route, in awake patients with normal muscle tone or if the mandible of the anaesthetised patient is held well forward. The bronchoscope is a valuable aid to intubation for patients with cervical fracture but its use requires practice and anaesthetists should endeavour to familiarise themselves with the technique.

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S.R. FINFER
J.M. SADDLER

A reply

Thank you for the chance to reply to Drs Finfer and Saddler. We readily concede that a smooth, awake, fiberoptic intubation is the ideal way to deal with a patient with an unstable cervical fracture and a full stomach. In an emergency, however, theory and practice sometimes meet head on and one has to take into account one's own competence and the patient's state of mind in making a realistic risk-benefit analysis of one's proposed technique. In the case described we were afraid that an attempt at awake intubation performed against the wishes of a heavily pregnant, nauseated and very frightened patient, was likely to lead to coughing, struggling and possibly vomiting.

It is apparent that Drs Finfer and Saddler are skilled in the technique of awake fiberoptic intubation, and the successful management of the first case they describe vindicates their point of view. (The second case is perhaps less relevant to the matter under discussion, since the patient was unconscious and quadriplegic and no topical anaesthesia or sedation were required.) We accept their criticisms as fair comment; smooth, awake intubation uncomplicated by coughing and gagging is, regrettably, the exception rather than the rule in our hands.

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J.R. EASON
C.N. SWAINE

Hypocarbica and eye surgery

We recently studied 47 patients over 65 years of age anaesthetised for cataract surgery, who were randomly allocated into two groups. The patients in both groups received controlled ventilation of the lungs, one group to an end tidal CO₂ of 3 kPa and the other, to an end tidal CO₂ of 5 kPa. Anaesthesia was otherwise identical in the two groups; drugs were given on a mg/kg basis. After pre-oxygenation patients were induced with fentanyl and etomidate, an intubating dose of atracurium was given and controlled ventilation commenced with 40% oxygen-60% nitrous oxide via a Penlon Oxford ventilator fitted with a circle system but without a CO₂ absorber. The ventilator was set to deliver a tidal volume of 12 ml/kg at a rate of 15 breaths/minute. End tidal CO₂ was controlled by adjustment of the fresh gas flow, and measured with a Gould capnograph Mk3. The sampling rate was set to give a satisfactory end tidal plateau. Gas was sampled at the tracheal tube connector. Anaesthesia was maintained with nitrous oxide supplemented by 0-2% enflurane, and relaxation maintained by boluses of atracurium. Each patient received intramuscular prochlorperazine.

The surgeon, who was unaware of the anaesthetic details, was asked to assess operating conditions as good, satisfactory or poor at the end of the operation. The operating conditions were good or satisfactory in 93.6% of procedures. Statistical analysis was by the Chi-square test or Fisher's

exact test as appropriate, and showed no statistically significant difference between the groups (Table 1).

Table 1. Operating conditions.

	Good	Satisfactory	Poor	Total
Normocapnic	13	4	1	18
Hypocapnic	19	8	2	29

These results show that in elderly patients for cataract surgery who receive controlled ventilation of the lungs supplemented by a volatile anaesthetic, good operating conditions can be provided with no need to utilise hypocarbica. The work of Zindel¹ probably explains why this is so and indicates that the above observation is probably true for eye patients of all ages.

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Stoke on Trent

B.H. YATE
N.P. CARTER
M.A. BOURNE

Reference

1. ZINDEL G, MEISTELMAN C, GAUDY JH. Effects of increasing enflurane concentration on intra-ocular pressure. *British Journal of Anaesthesia* 1987; 59: 440-3.

Pain-free intravenous injections

We read with interest the letter from Dr Porteous (*Anaesthesia* 1987; 42: 1021). The findings support those of a double-blind study conducted in this hospital on the pain of injection of methohexitone, the results of which we neglected to publish.

Hospital ethical committee approval was obtained and the 88 patients studied were randomly allocated to receive 2 ml of either 1% lignocaine or normal saline from numbered ampoules prepared by the pharmacy department. All subjects were either unpremedicated or premedicated with a benzodiazepine with or without an anticholinergic agent. The anaesthetist responsible for the case injected this solution via an indwelling needle in the dorsum of the subjects' non-dominant hand whilst the subjects' forearm was gripped one hand breadth above the wrist. Venous occlusion was maintained for 30 seconds after injection of this solution. The methohexitone was then administered and when 75% of the anticipated induction dose had been given, patients were questioned about the sensation in their

arm and asked to grade it as painless, mild, moderate or severe pain. One patient was anaesthetised before he gave his response. The anaesthetist was also asked to grade the patients' response as none, minimal or obvious pain, prior to questioning.

There was no significant difference between the groups in terms of age, sex or the pattern of premedication. However, the group that received lignocaine showed a lower incidence of discomfort assessed by both the subject and the anaesthetist (Table 1). An identical study which involved 63 patients, conducted without venous occlusion tourniquet, failed to show any significant difference between the groups. This has become our routine practice and, like Porteous, we have never seen any complications as a result.

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P.J. HEATH
A.J. PEARCE
M. HANKOVA
H.L.R. BASTIAENEN

Table 1. Discomfort assessed by patients and anaesthetist during injection of methohexitone.

	Patients' assessment *				Total	Anaesthetist's assessment †			Total
	Painless	Mild discomfort	Moderate discomfort	Severe discomfort		None	Minimal discomfort	Obvious discomfort	
Lignocaine	31	6	2	2	41	36	2	3	41
Saline	17	9	11	9	46	24	6	17	47

* $\chi^2 = 11.2$, $p < 0.025$.
† $\chi^2 = 13.87$, $p < 0.005$.

Spinal anaesthesia after facet joint injection

We were interested to see the report by Goldstone and Pennant (*Anaesthesia* 1987; 42: 754-6). Our experience suggests that the most likely mechanism is penetration of the needle right through the facet joint, and consequent intrathecal injection.

We have on two occasions aspirated free-flowing cerebro-

spinal fluid (CSF) through a needle which was radiologically located centrally in the joint cavity using the same technique as described in the article. CSF, in another patient, was seen to drip spontaneously from a needle through which nothing could be aspirated, and a faint and evanescent radiculogram appeared on the image intensifier monitor on

injection of contrast medium. Satisfactory placement was achieved on each occasion simply by withdrawal of the needle by 1 or 2 mm, and the infiltration was performed uneventfully.

The anterior facet joint capsule is formed by the ligamentum flavum,¹ so it is very probable that over-penetration of the joint will result in intrathecal injection. We strongly support the recommendations of Goldstone and Pennant about the availability of resuscitation equipment. In addition, we suggest that bony contact with the most posterior part of one of the articular facets should be deliberately sought during needle placement, to act as a 'depth gauge' for subsequent needle advancement which should be no more than 2 or 3 mm beyond this level. It is interesting that the authors' use of low-volume facet arthrography did not prevent this complication. We have found the images obtained by facet arthrography to be sometimes difficult or impossible to interpret with confidence, even when volumes of 0.5–1 ml contrast medium are employed. Frequent aspiration is prudent even after unequivocal arthrography, since most patients tend to shift position during this uncomfortable procedure and might perhaps disturb the needle tip by so doing.

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A.J. SEMPLE

Reference

1. LEWIN T, MOFFETT B, VIIDIK A. The morphology of the lumbar synovial intervertebral joints. *Acta Morphologica Neerlando-Scandinavica* 1962; 4: 299–319.

A reply

Thank you for the opportunity to reply to Drs Marks and Semple. It is our normal practice to penetrate until bony resistance is both felt, and visualised on the image intensifier, and then to withdraw the needle; we also aspirate and look for clear fluid to indicate CSF. This we consider to be good practice for any needle technique, more especially when close to the neuraxis.

The result was negative in both cases reported. We think that in our cases it is likely that the needle was endoneural rather than intrathecal. Subsequent injection produced the catastrophic collapse of both patients. We repeat our recommendation that resuscitation facilities should be available immediately whenever these nerve blocks are performed.

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J.C. GOLDSTONE

Anaphylactoid reaction to oral premedication with temazepam and promethazine

There are few reports of allergy or anaphylactoid reaction to these drugs.^{1,2} Promethazine has caused stridor, wheeze and urticaria one hour after ingestion,² while skin rash and urticaria^{3,4} may follow treatment with benzodiazepines. There have been more serious reactions: in one of these, an anaphylactoid reaction,⁵ the cause was perhaps cremophor EL;⁶ no causal relation was established for the loss of consciousness in the other.⁷

A 39-year-old female was admitted for reversal of sterilisation. She showed no indication of abnormal responses to any of the drugs that were given to her in the course of six previous general anaesthetics. Her general health was good and her only medication was norethisterone. She gave a history of swelling of the face and tongue when as a child she was given oral penicillin, but there was no history of any drug allergy. Of her five children, one is 'allergic to aspirin', two have asthma and one has eczema.

Oral premedication was with promethazine 25 mg and temazepam 30 mg. She complained of burning skin, a tight throat and chest, palpitation and generalised itching within 15 minutes and she experienced a sudden urge to defaecate and to micturate. The ward staff noticed that she had turned pink all over. She lost consciousness 20 minutes after premedication; the systolic blood pressure was 60 mmHg and there was a tachycardia of 120 beats/minute. Resuscitation by the medical team consisted of oxygen by face-mask, intravenous normal saline 1000 ml, polygeline 500 ml, chlorpheniramine 10 mg and hydrocortisone 100 mg. The patient recovered consciousness 15 minutes later without the need for tracheal intubation or adrenaline. She was managed on the ward uneventfully. Facial oedema was still present the next day. She could not remember the period of resuscitation.

Further enquiry revealed that she had taken numerous benzodiazepines and phenothiazines at various times in the past, although she had never had temazepam. She had previously received promethazine in both oral and intramuscular forms with no adverse effect.

Skin tests were done on readmission 2 weeks later, to temazepam, promethazine and to the dyes and bases of their formulation. Promethazine tablets (May and Baker

Ltd) contain Brilliant Blue in a sucrose base; for temazepam (Wyeth Laboratories) Quiniline Yellow is the dye, which contains titanium oxide. The temazepam capsule contains gelatin and the promethazine tablet base includes lactose, kaolin and dextran. Skin tests with the drugs, dyes and bases at dilutions from 1:10,000 up to 1:10 were negative. An uneventful premedication with papaveretum and hyoscine preceded an uneventful anaesthetic for reversal of sterilisation.

This unusual reaction to oral premedication with these common preparations reminds us all that no drug is free from adverse effects, and that no drug should be considered free from 'extra ingredients' which might also produce adverse reactions. It follows that the more medications a patient receives, the greater is the risk of a rare, but life-threatening reaction. The skin tests were negative (which suggests a mechanism involving an alternative pathway of activating complement; that is, not involving formation of antibody/antigen complexes), so the agent responsible remains unidentified.

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References

1. MARTINDALE. *Extra pharmacopoeia*, 28th edn. London: Pharmaceutical Press, 1982: 1294.
2. TESTER-DALDERUP CBM. In: DUKES MNG, ed. *Antihistamines. Side effects of drugs, Annual 9*. Amsterdam: Elsevier, 1985: 152–3.
3. JERRAM T. In: DUKES MNG, ed. *Hypnotics and sedatives. Mayler's side effects of drugs*, 10th edn. Amsterdam: Elsevier, 1984: 82.
4. BROGGER NIELSEN F. Anaphylactic reaction to Diazemuls. *British Journal of Anaesthesia* 1984; 56: 1179.
5. MILNER L. Allergy to diazepam. *British Medical Journal* 1977; 1: 144.
6. PADFIELD A, WATKINS J. Allergy to diazepam. *British Medical Journal* 1977; 1: 575–6.
7. FOWLER LK. Temazepam (Euhypnos) as a hypnotic: a twelve-week trial in general practice. *Journal of International Medical Research* 1977; 5: 295–6.

Arterial oxygen saturation during general anaesthesia for dental extraction in children

Dr Bone and colleagues (*Anaesthesia* 1987; 42: 879–82) showed that a significant degree of hypoxia occurs in 50% of children anaesthetised with an inspired concentration of 33% oxygen. A previous study by Walsh¹ also showed hypoxia which was an even greater problem when the inspired concentration was lower, at 25% and 20%.

Nunn² showed in 1964 that an inspired concentration of 35% was needed to prevent hypoxia in a series of patients breathing spontaneously and, since then, I have advocated a concentration of 50% inspired oxygen in dental anaesthesia for children;^{3–5} the added 15% gives a safety margin and prevents hypoxia should any temporary airway obstruction occur during the dental extractions. The nitrous oxide percentage is lowered by this technique from 65% to 50% but, in terms of minimum alveolar concentrations, this can be compensated for by a 0.1% increase in halothane concentration.

There is no need for the use of an inspired oxygen percentage less than 50% during dental outpatient anaesthesia.

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References

1. WALSH JF. Training for day-case dental anaesthesia. Oxygen saturation during general anaesthesia administered by dental undergraduates. *Anaesthesia* 1984; 39: 1124–7.
2. NUNN JF. Factors influencing the arterial oxygen tension during halothane anaesthesia with spontaneous respiration. *British Journal of Anaesthesia* 1964; 36: 327–41.
3. LATHAM JW, PARBROOK GD. Premixed gas machine. *Anaesthesia* 1967; 22: 316–21.
4. LATHAM JW, PARBROOK GD. The use of pre-mixed nitrous oxide and oxygen in dental anaesthesia. A clinical trial of the 50/50 mixture in general dental practice. *Anaesthesia* 1966; 21: 472–9.
5. PARBROOK GD. Training for day-case anaesthesia. Oxygen saturation during general anaesthesia administered by dental undergraduates. *Anaesthesia* 1985; 40: 377.

A reply

Thank you for the opportunity to reply. In our study the recorded episodes of hypoxia were associated with procedures which resulted in airway obstruction and their severity was greater when the anaesthesia was administered by a supervised dental student. A perfect anaesthetic technique is difficult to obtain and some degree of airway obstruction may be inevitable even with experienced personnel. We agree that increasing the inspired oxygen concentration to 50% may reduce the extent of decreases in SaO_2 , although it cannot guarantee prevention of hypoxia from failure of airway technique. We found dental undergraduates were slower to recognise airway obstruction and to take remedial action and, indeed, studies undertaken by Dr Parbrook^{1,2} did not include dental undergraduates but only experienced anaesthetists.

Surely the important fact is the early recognition of hypoxia or airway obstruction and its prompt rectification. In addition to observations of patient colour and the reservoir bag, the ECG is now considered to be the minimal monitoring requirement during dental outpatient extractions. However, none of these detects the early but significant decreases in SaO_2 , especially in dark-skinned patients. We would suggest that oximetry now be considered part of this minimal monitoring.

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M.E. BONE
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References

1. LATHAM JW, PARBROOK GD. The use of pre-mixed nitrous oxide and oxygen in dental anaesthesia. A clinical trial of the 50/50 mixture in general dental practice. *Anaesthesia* 1966; 21: 472–9.
2. PARBROOK GD. Training for day case anaesthesia. Oxygen saturation during general anaesthesia administered by dental undergraduates. *Anaesthesia* 1985; 40: 377.

A paediatric scavenging valve

Most suggestions for disposal of the gas flow from the Jackson-Rees modification of Ayre's T-piece affect the convenience of the system. Previous authors have described the use of a circle-absorption unit,¹ co-axial tubing attached to the reservoir bag outlet² and transparent enclosure of the conventional Dennison valve (*Anaesthesia* 1987; 42: 439–40). We have found that a scavenging connector and a readily available drainage tap can be fitted together to provide a fully versatile attachment for the outlet of a paediatric breathing system. Several of these connectors have been in use here for 18 months.

The rotating control from an overnight drainage bag (Bard) replaces a reservoir bag tail valve, if one is normally used, and is secured using sections of bubble tubing (Argyle) to the 22-mm port of a standard 30-mm ISO male taper hose adaptor (Penlon) (Fig. 1). This is drilled to allow air to be entrained when used with active scavenging equipment. Exhaust gases are removed by attaching a female adaptor and tubing. The minimum resistance to gas flow with air, 0.059 kPa at 10 litres/minute, is close to that of the Dennison valve, 0.049 kPa at 10 litres/minute; each can, of course, be turned towards occlusion. It is not easily broken and the long probe when properly inserted is unlikely to obstruct. One-handed lever control makes these

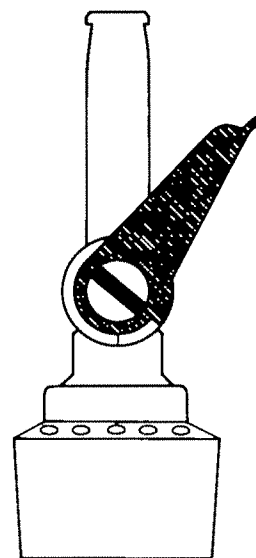


Fig. 1. Diagram of valve and connector.

more satisfactory than any other arrangement that restricts the opening (Fig. 2) including those which use adhesive tape or surgical clips.

Further improvements can be made if the orientation of the lumen is indicated on the valve hub, the barrel is reversed and the stops taken back so that closure is achieved in either direction, and if angles are cut in the sides of the rotating orifice. The maximum pressure that can occur during anaesthesia is then reduced to the order of 3 kPa at a fresh gas flow of 4.5 litres/minute.

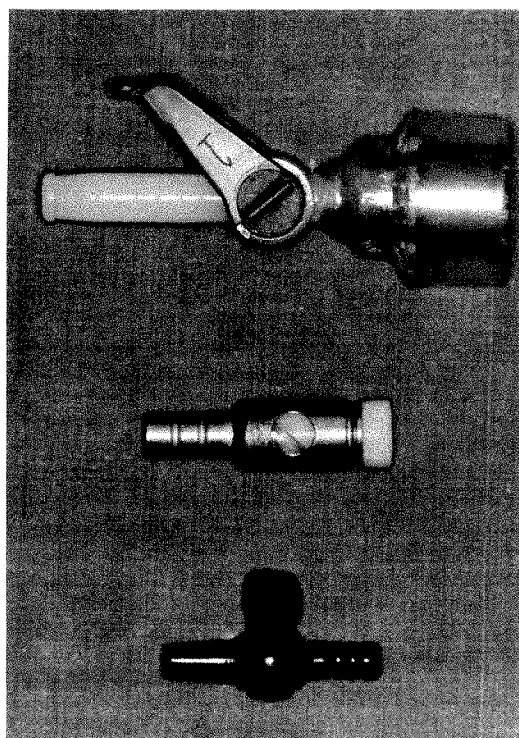
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M.R. NOTT

References

1. ALBERT CA, KWAN A, KIM C, SHIBUYA J, ALBERT SN. A waste gas scavenging valve for pediatric systems. *Anesthesia and Analgesia* 1977; **56**: 291-2.
2. FLOWERDEW RMM. Coaxial scavenger for paediatric anaesthesia. *Canadian Anaesthetists' Society Journal* 1979; **26**: 367-9.

Fig. 2. Improved version, Dennison valve and vulcanite tap.



Distress caused by urethral catheters

Dr Coates' apparent success (*Anaesthesia* 1986; **41**: 670) with the instillation of bupivacaine into the bladder to relieve the distress caused by urethral catheters, was interesting but I would like to add a note of caution and cynicism from my own experience.

A 75-year-old woman was admitted here with advanced carcinoma of the bladder that caused pain (which she perceived as in the bladder), urinary frequency and dysuria, in spite of an indwelling catheter. The pain was resistant to opiates but her symptoms responded partly to the twice daily instillation of 1% lignocaine, and subsequently responded completely to 2% lignocaine.

A double-blind placebo controlled trial over 6 days showed no difference in symptoms (assessed by simple analogue scale), between the days she received lignocaine and the days she received placebo normal saline. Both

solutions had a better effect if they were cooled. It seems unlikely that we have produced the long-term benefit reported with bupivacaine because lignocaine is a much shorter-acting drug.

We therefore concluded that our patient benefitted from attention to her symptoms together with the introduction of a soothing, cooled solution into the bladder. A similar study needs to be conducted before the benefits are attributed to local anaesthesia.

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S. DOVER

Editor's note. The publication of this letter has been unavoidably delayed.

A cause of apparent resistance to thiopentone

Unanticipated resistance to thiopentone occurs occasionally. Recently a vial of thiopentone powder was noticed to be surprisingly empty. It is, of course, standard anaesthetic practice to check the label of ampoules prior to use and any loss of volume is immediately obvious. How often do anaesthetists similarly assess the contents of vials that contain powder for reconstitution? Perhaps a less obviously empty vial could have been overlooked in the cases just mentioned.

The vial was assayed by the North West Regional Quality Control Laboratory and found to contain 25 mg of thiopentone sodium and, if used, would have produced a solution only 5% of the stated strength.

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P. NIGHTINGALE

A reply

In reply to Dr Nightingale's observations, we are very concerned that a vial of thiopentone sodium 0.5 g could have

been manufactured and subsequently released for use with only 25 mg of the active substance present.

As a Company, we manufacture approximately one million vials of thiopentone sodium each year. Despite the considerable and rigorous quality monitoring throughout the vial filling and labelling process, where every effort is made to prevent such an occurrence as the above from happening, atypical events can unfortunately occur. Such events should be extremely rare but we can only support Dr Nightingale's suggestion that the anaesthetist, when checking the label, makes an assessment of the vial's contents prior to reconstitution. Obviously, this incident has prompted both my quality and production colleagues to reinforce the need for vigilance to all concerned in every stage of manufacturing control.

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K. DOBSON

Epidural catheter migration during labour

I applaud Drs Phillips and Macdonald (*Anaesthesia* 1987; 42: 661-3) for their most valuable study of epidural catheter migration and agree most heartily with their final assertion that there is no room for complacency in the organisation of an epidural service. To misquote: the price of safety is eternal vigilance.

I am interested to hear that, as a result of their experiences of inward migration of catheters, Drs Phillips and Macdonald suggest that a catheter with a single end hole may be safer than one with three helical holes. There are many reports both in the literature and *sub judice* of failed aspiration tests for both subarachnoid and intravascular catheter placement, particularly from the US¹⁻³ where single end hole catheters are in widespread use. A moment's reflection suggests that such false negatives are more likely to occur with a single- than with a three-holed catheter. Moreover, the work of Hardy⁴ suggests that an epidural catheter cannot by itself penetrate the dura mater, though it may penetrate the arachnoid if the needle has first penetrated the dura. I can understand that in the cases cited by Drs Phillips and Macdonald, one catheter migrated into a previously penetrated blood vessel and another through the arachnoid following presumed needle penetration of the dura, but I would be surprised if the use of a single end hole catheter would necessarily have avoided both of these mishaps.

There has been no case of intravascular catheter insertion

that was not diagnosed at once on aspiration (as was the Leeds one) in 11 000 obstetric epidurals using three-holed catheters in this hospital, and only one in which a spinal headache followed an apparently uneventful epidural with four successful and harmless top-up doses. This headache started abruptly 48 hours post partum and required a blood patch to cure it.

There is clearly a need for an extensive, randomised, controlled trial of the two catheter types before we all convert to the single end hole type of catheter. I would be interested to hear if any such has been instituted.

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F. REYNOLDS

References

1. RAVINDRAN RS, BOND VK, TASCH MD, GUPTA CD, LUESSEN TG. Prolonged neural blockade following regional analgesia with 2-chloroprocaine. *Anesthesia and Analgesia* 1980; 59: 447-51.
2. REISNER LS, HOCHMAN BN, PLUMER MH. Persistent neurologic deficit and adhesive arachnoiditis following intrathecal 2-chloroprocaine injection. *Anesthesia and Analgesia* 1980; 59: 452-4.
3. MOORE DC, SPIERDIJK J, VANKLEEF JD, COLEMAN RL, LOVE GF. Chloroprocaine neurotoxicity: four additional cases. *Anesthesia and Analgesia* 1982; 61: 155-9.
4. HARDY PAJ. Can epidural catheters penetrate dura mater? An anatomical study. *Anaesthesia* 1986; 41: 1146-7.

Respiratory arrest after sufentanil

Sufentanil has been used in our department as the opioid of choice for extradural pain relief (about 3 000 injections) for more than 3 years. The duration of analgesia varies from 4 to 10 hours; peak plasma levels are noted between 5 and 20 minutes following administration.^{1,2}

Extreme bradypnoea within 15 minutes after injection was observed in two subjects. In both instances sufentanil 50 µg diluted in 10 ml 0.9% saline was injected after a thoracotomy, during which intravenous morphine 0.3 mg/kg was used for perioperative analgesia. Effective pain relief may improve breathing quality but this beneficial effect was dominated by opioid-induced sedation and hypoventilation. Both patients became unresponsive; their condition was probably aggravated by P_{CO_2} levels that exceeded 12 kPa and required reintubation of the trachea and artificial ventilation of the lungs.

However, the second injection 6 hours later was uneventful. Sufentanil levels measured in the first patient during these two injections revealed peak values of 0.26 ng/ml and 0.24 ng/ml at 10 minutes. These levels are within the normal range compared with other studies.² Therefore, we assume that the respiratory problems were due to systemic resorption in weak patients not sufficiently awake and with compromised pulmonary function. This is consistent with the similar conclusions of Ahuja and Strunin,³ who studied the respiratory effects of epidural fentanyl after systemic morphine administration.

These two experiences did not force us to give up the use of sufentanil. Late and unpredictable respiratory arrest, as described with morphine, was not observed. This may be explained by the lipophilic properties of sufentanil and hence a limited rostral spread. Respiratory problems may occur occasionally but not more than 20 minutes after administration. Therefore, the first injection should be administered in the recovery room or in the ICU and side effects should be sought carefully during the first 20 minutes following each injection.

The first patient reported by Blackburn⁴ also had some pre-existing pulmonary problems. In the second case the interval between the injections was clearly too short (seven doses in 22 hours). In these circumstances we would have considered the addition of adrenaline (epidurally) or naloxone (intravenously).

Plasma samples taken in our department in six patients during abdominal surgery, showed sufentanil levels between 0.05 and 0.10 ng/ml at 180 minutes which decreased to less than the detection level at 240 minutes. A possible cumulative effect should be taken into consideration when a re-injection is required less than 4 hours after the previous dose.

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References

1. VERCAUTEREN M, MOENS F, HANEGREEFS G. Modification of analgesic quality and side effects of epidural sufentanil. In: SCHERPEREEL PH *et al.*, eds. *The pain clinic. II*. Utrecht: VNU Science Press, 1987: 299-301.
2. TAN S, COHEN MB, WHITE PF. Sufentanil for analgesia after cesarean section: intravenous versus epidural administration. *Anesthesia and Analgesia* 1986; 65: S158.
3. AHUJA BR, STRUNIN L. Respiratory effects of epidural fentanyl. Changes in end-tidal CO_2 and respiratory rate following single doses and continuous infusions of epidural fentanyl. *Anaesthesia* 1985; 40: 949-55.
4. BLACKBURN C. Respiratory arrest after epidural sufentanil. *Anaesthesia* 1987; 42: 665-6.

A reply

Thank you for the opportunity to reply. The point in my letter was the unpredictable response to 'top-up' doses of epidural sufentanil. This suggests that careful monitoring is required following every dose.

We have had another case of respiratory arrest after sufentanil. This occurred in an elderly patient following

abdominal surgery, whose first dose of epidural sufentanil was uneventful but who stopped breathing after a second dose given 13 hours later.

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C. BLACKBURN

Allergy to propofol?

A 40-year-old Asian female with a history of asthma and eczema presented as a day case for incision and drainage of an abscess on her left shoulder. She required a repeat procedure one week later. The general anaesthetic on each occasion consisted of intermittent bolus injections of propofol, nitrous oxide and oxygen. Lignocaine 5 mg was mixed with the propofol on the first occasion but excluded on the second. No other drugs were given during the anaesthetic nor were any antibiotics prescribed.

She developed an itchy rash on her neck, head and scalp within 24 hours following both procedures. There were no other symptoms. The rash appeared later that evening, approximately 12 hours after injection on the second exposure. The rash appeared as numerous erythematous papules (5 mm–1.5 cm in diameter) distributed over the head and neck when it was seen 3 days after the second anaesthetic. None were present elsewhere. The rash persisted for 3 days on the first occasion and 9 days on the second.

She had no adverse reactions to other anaesthetics despite the history of atopy. She was not allergic to eggs or other foodstuffs. The development of a rash in an atopic individual following anaesthesia suggests an allergic phenomenon and

in this case, where rechallenge evoked an identical reaction, a fixed drug eruption to propofol, a metabolite or the vehicle appears to have been the cause.

Photosensitivity is a possible mechanism, although the dorsum of the hands were spared. The patient reported more itching when exposed to the sunlight. Transitory rashes following intravenous bolus administrations of propofol are not uncommon¹ but a delayed onset has been reported in only one patient who received several drugs.² This case has been reported to ICI who will notify the Committee on Safety of Medicines.

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References

1. DOENICKE A, LORENZ W, STANWORTH D, DUKA TH, GLEN JB. Effects of propofol (Diprivan) on histamine release, immunoglobulin levels and activation of complement in healthy volunteers. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 15–20.
2. ICI Product Information.

A modified split tongue retractor

The recent correspondence by Drs Buckley and Bush (*Anaesthesia* 1987; **42**: 778) highlighted the potential problems associated with the mismatching of sizes of RAE tracheal tubes when used with the Doughty split tongue retractor. Failure to use the correct size can result in herniation of the tube through the slot. A simple modification to the split retractor is in routine use here since the occurrence of a herniation as described.

The gags are modified by fitting two 'bars' across the top of the blade, as illustrated on the three sizes of retractor (Fig. 1). This easily performed modification has proved entirely practical and minimises the possibility of herniation whilst it maintains the advantages of a split retractor.

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B.C. SELICK

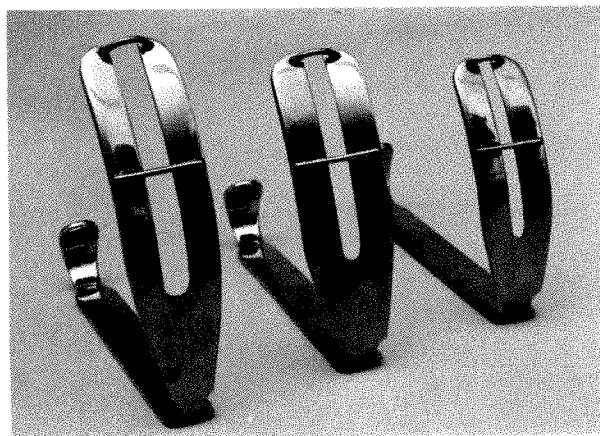


Fig. 1.

Risks of infection from water bath blood warmers

Dr Bray (*Anaesthesia* 1987; **42**: 778) observed that the water in blood warming baths in one institution was contaminated with an assortment of bacteria and, in contrast to the paucity of clinical reports in support of the contention that contamination leads to septicaemia during the use of blood warming baths, recommends a nostrum that may be difficult to accept, namely, that 'in view of the potential risk to patients we should not use water bath blood warmers but dry heat exchangers'.

There are several points that merit attention. Firstly, a

cause-effect relationship was not established by this limited study. Secondly, most commercial blood warming coils are manufactured to ensure that injection ports and joints do not occur in the vicinity of the warming bath. Where an extension set¹ is used for blood warming one would expect the user to exercise common sense and to ensure that joints were outside the warming bath.

Finally, it is worth emphasis that the use of disposable blood warming devices (immersible coils as well as dry heat exchangers) in routine surgery when blood products are

usually administered at a rate less than 25 ml/minute, does not help to maintain body temperature. It was found in a study² of patients who received blood via disposable blood warming devices, that patient input temperatures were only 0–2°C above operating room temperatures. This suggests a wasteful use of expensive blood warming equipment. The writer has already shown¹ that there is no advantage in using a disposable blood warming device when the rate of blood transfusion is less than 25 ml/minute. In fact, higher patient input temperatures can be achieved simply by immersing the intravenous tubing in a warming bath. King and Davis³ found that extension sets may provide adequate warming of crystalloids up to a flow rate of 55 ml/minute.

Account should therefore be taken of the anticipated flow rate before resort to the use of expensive fluid warming

devices. An extension device should be used for fluid warming if the flow rate is unlikely to exceed 30 ml/minute.

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H. VAGHADIA

References

1. VAGHADIA H. Blood warming with the Avon A60 extension set. *Anaesthesia* 1984; **39**: 932–3.
2. VAGHADIA H. Blood warming devices do not guarantee temperature homeostasis. *Anesthesiology* 1986; **65**: 237–8.
3. KING S, DAVIS FM. Infusion fluid warming. *Anaesthesia and Intensive Care* 1985; **13**: 440.

Bradycardia during intra-abdominal surgery

It was interesting to read (*Anaesthesia* 1987; **42**: 835–9) of Drs Coventry, McMenamin and Lawrie's experience of bradycardia that occurred during abdominal operations whilst the newer muscle relaxing drugs were in use. In 1957, in an article entitled 'Inadequacy of general anaesthesia for abdominal operations',¹ I described bradycardia, hypotension, pallor and sweating during abdominal operations when the anaesthetics given were thiopentone, tubocurarine and nitrous oxide with oxygen. I showed that these untoward complications were due to autonomic stimulation and could be stopped by autonomic blockade by means of local anaesthetic injections.

I eventually gave up these injections as a routine for all major abdominal operations and treated the complications as they arose, since the autonomic stimulation occurred in only 20–30% of cases and since the local anaesthetic injections, possibly dangerous in their own right, had to be given to all cases because there was no way to tell which patient would so react.

You may imagine my delight when I changed relaxant to pancuronium bromide and found that the bradycardia and other complications no longer occurred. Pancuronium is said to have a weak vagolytic action, which tubocurarine has not and neither presumably have the newer muscle relaxants. If they are to be used then presumably some form of anti-autonomic stimulation should be given.

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Reference

1. LODER RE. Inadequacy of general anaesthesia for abdominal operations. A possible solution. *Lancet* 1957; **2**: 468–70.

Failure of external cardiac compression

A case is described in which external cardiac massage was ineffective in the production of a satisfactory cardiac output.

A 66-year-old man was to undergo a lower third oesophagectomy for carcinoma. Anaesthesia proceeded uneventfully during laparotomy for mobilisation of the stomach. The patient was then turned into a right lateral position for thoracotomy. The ECG showed sinus bradycardia of 40 beats/minute and no pulses were palpable at this moment. Atropine 1.2 mg was given, the patient replaced supine and external cardiac massage begun. No pulses could be felt but there was no obvious reason why external massage was ineffective. Ventilation of the lungs was difficult. Tracheal suction yielded copious blood-stained mucus, after which ventilation was satisfactory. The cardiac massage remained ineffective so the surgeon was persuaded to re-open the abdomen and combine a check for bleeding with direct cardiac massage through the open diaphragm. A pulse was immediately felt, spontaneous heart activity returned within 30 seconds and the operation proceeded to completion.

None of the causes of an obstructed circulation, such as cardiac tamponade or pulmonary embolism, was present nor was he exsanguinated. The probable reason for failure of external cardiac compression was the large surgical defect

in the diaphragm. It is likely that the heart acts as a conduit during external cardiac massage. The increase in intra-thoracic pressure with massage could be dissipated through an open diaphragm. External support of the abdomen during massage might have produced a satisfactory output.^{1,2}

This case provides a practical demonstration of the passive role of the heart during external cardiac compression and of the importance of integrity of the thorax. Rapid introduction of internal massage may be of value in case of difficulty with any patient with a disrupted chest wall or diaphragm.

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D.J. GREAVES

References

1. GREENBERG M, GENRNER M, ROBERTS J. *Advanced techniques in resuscitation*. Baltimore: Williams and Wilkins, 1985.
2. NIEMANN JT, ROSBOROUGH J, HAUSKNECHT M, BROWN D, CRILEY JM. Cough-CPR: documentation of systemic perfusion in man and in an experimental model: a 'window' to the mechanism of blood flow in external CPR. *Critical Care Medicine* 1980; **8**: 141–6.

Sodium bicarbonate solutions

With reference to Dr Dumont's letter (*Anaesthesia* 1987; 42: 1018), until a few years ago Boots produced a 100-ml bottle of 8.4% NaHCO_3 . This was ideal for cardiac arrests, because serious overdosage was unlikely; it was given as an infusion and could be repeated if necessary. This was withdrawn for economic reasons. 100-ml bags of saline are now widely available so why can similar bags of 8.4% NaHCO_3

not be produced to replace the potential overdosage represented by the Polyfusor bags? This might also serve to lessen the severe tissue damage caused by an extravasated freely running infusion.

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R.L. HUGHES

Confirmation of tracheal tube placement

The report by Drs Charters and Wilkinson (*Anaesthesia* 1987; 42: 801-7) gives me the opportunity to describe another, rather underused tactile method for determining the correct placement of tracheal tubes. The cuff is inflated in the normal manner until any leak of gas is abolished following insertion of the tracheal tube. Two fingers are placed in the suprasternal notch and a further 5 ml of air is introduced rapidly into the cuff. An outward force will be felt by the fingers in the notch if the tracheal tube is in the correct position. Indeed, a recent study¹ showed that this method not only confirms tracheal placement of the tube, but also that the tube is in the optimal position within the trachea, that is, not too near the carina or down one main bronchus. This simple, rapid and reliable technique provides another useful tool in the fight against inadvertent oesophageal intubation.

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Reference

1. EHRENWERTH J, NAGLE S, HIRSCH NP, LAMANTIA K. Is cuff palpation a useful tool for determining endotracheal tube position? *Anesthesiology* 1986; 65: A137.

A reply

Thank you for the opportunity to comment on the letter from Dr Hirsch. His paper was published after ours was submitted for publication. This paper is timely because, as our own paper states, clinical tests used to confirm tracheal tube placement 'have received little objective scrutiny to determine their reliability'. We note that auscultation of the lungs and observation of chest movement resulted in optimal positioning of the tracheal tube in only 85% of cases.

Anaesthetists have only relatively recently become aware of the importance of how uncertain these tests can be. This realisation has occurred because a small number of courageous clinicians have, in effect, put their own reputations on the line to convince fellow anaesthetists that the tests can really be misleading. We suggest that there are some general points in the assessment of any test to confirm tracheal tube placement.

The test should work in difficult intubations. These are relatively uncommon so much of the evaluation of these tests will continue to be done in patients who are not difficult. This allows the possibility of a description of a test which is not particularly relevant. A test described by Ford¹ involves a manoeuvre to displace the larynx posteriorly toward the palate, so allowing the cords to come into view

when they are not seen at the time of intubation. One of us (P.C.) has had the opportunity to assess this test in four cases of difficult intubation and it failed in every case. It now seems likely that, in effect, there can be no manipulation invoked in doing this test which should not have already been performed prior to the decision that the case was difficult in the first place.

Positive tests need to be unequivocal. Many of the tests have in our opinion a serious disadvantage which we describe as an analogue scale of positivity. The most obvious example is breath sounds. Imagine that it was possible to show that good breath sounds were a reliable sign of tracheal intubation. We would still need to be sceptical of what to describe as 'good' and how to interpret the whole spectrum of 'not so good' to 'not good at all'. Our test requires a very specific definition of positive, i.e. the delineation of all the boundaries of the interarytenoid groove and the relationship of the tracheal tube immediately anterior to it. Anything else is deemed not to be a positive sign.

Oesophageal intubation must never give a false positive sign. Unfortunately many of the standard tests do not fulfil this most important requirement.² Neither Hirsch nor others who have commended this test recently^{3,4} describe what happens when the tube has been misplaced in the oesophagus. In the case report by Stirt⁵ the inflated tracheal tube cuff was considered to be palpable at the sternal notch when it was later shown to have been in the oesophagus. We remain convinced after two years' experience of our test that a false positive test is very unlikely.

Clinicians using the tests must understand what they mean. Our test indicates that the tube lies within the trachea; it gives no information as to how far down the trachea it is. (We believe it should be possible to improve on this in the near future.) Most tests require interpretation and the clinician should be aware what the test actually indicates so that wrong conclusions are not drawn in an emergency.

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References

1. FORD RWJ. Confirming tracheal intubation—a simple manoeuvre. *Canadian Anaesthetists' Society Journal* 1983; 30: 191-3.
2. BIRMINGHAM PK, CHENEY FW, WARD RJ. Esophageal intubation: a review of detection techniques. *Anesthesia and Analgesia* 1986; 65: 886-91.
3. TRINER L. A simple maneuver to verify proper positioning of an endotracheal tube. *Anesthesiology* 1982; 57: 548-9.
4. MUNRO TN. Oesophageal misplacement of a tracheal tube. *Anaesthesia* 1985; 40: 919-20.
5. STIRT JA. Endotracheal tube misplacement. *Anaesthesia and Intensive Care* 1982; 10: 274-6.

'Right at your finger tips'—is the oximeter only half the story?

The increasing popularity of transcutaneous oximetry highlights the fact that infrared transillumination of tissues, in the sequence of emission, absorption and detection, has

become firmly established. Infrared oximetry takes advantage of the maximum separation of the absorption curves for saturated and unsaturated haemoglobin in the 600 nm

and 900 nm ranges, in order to determine the relative quantities of each present and thence to display saturation percentage in a digital form. Some models of oximeter, using the same infrared source, also display the pulse wave either as a curve on an oscilloscope or as a small bar graph, but this form of display on oximeters is a secondary adjunct to the main purpose of the instrument.

Transcutaneous infrared detection dedicated purely to the monitoring of pulsatile cutaneous flow—quite apart from, and independent of, digital oximetry—is clinically useful in its own right when associated with an adequate form of display. Hitherto, for the lack of such a display, the clinically significant information to be gleaned from observation of variation in peripheral cutaneous blood flow through the pulp spaces of digits of patients undergoing anaesthesia, has not been adequately appreciated although it is there for the taking.

This is a description of the features of a prototype for a cutaneous blood flow monitor which fulfills these requirements qualitatively as an alerting device that draws attention to change, and which thereby fills a gap in the monitoring armamentarium. (Pulp space flow does not lend itself to meaningful direct quantification.) Ideally, the infrared emitter/sensor operates at the isobestic point, 805 nm, at which the degree of saturation of haemoglobin is irrelevant, and whereby the only variable is the mass of haemoglobin interposed along the light path of the emission. Pulsatile change in this mass causes pulsatile change in the absorption of the infrared radiation and thus in the light incident upon the sensor, in the photoresistance of the sensor and thence in the current flow within it. The sensitivity of this device is in the order of nanoamperes. This means that the slightest change in the amplitude of pulsatile flow is detectable and can be displayed. (The sensitivity of infrared devices exceeds the sensitivity of ordinary photoelectric cells that respond to visible light, particularly at very low light levels, which explains why pulse monitors based upon the latter have proved to be notoriously unreliable with weak pulses.) The signal passes through a pre-amplification circuit and is expressed as a varying voltage which is then fed to a 16-position analogue-to-digital integrated chip. The output contacts of this chip feed a horizontal row of light-emitting diodes (LEDs) such that the higher the peak of the pulse amplitude detected, the higher the voltage generated and the further to the right along the line of LEDs is the 'peak' LED that is illuminated. Each subset of four LEDs is subtended by an oblong panel light, from the left respectively red, amber, green and blue, and of sufficient brightness to be readily visible at a nurse's station from the far end of the ward.

A condenser lies at the electronic core of the device and is charged up by the peak voltage; it momentarily holds the voltage that relates to the peak LED. 'Peak pulse amplitude' is thus held on view as a steady display. However, the condenser bleeds through a resistor to earth, and so constantly attempts to discharge. If there is no further incoming signal after a particular beat, or if the next beat is of a lower

order, then, at a rate determined by the time constant set by the bleed resistor, the display will regress to the left, i.e. back towards the red sector, as a function of the progressive net discharge of the condenser. The device is thus fail safe. Conversely, an increase in peak pulse amplitude will cause the display to move to the right, towards the blue sector. A gain control enables the display to be set arbitrarily at an initial baseline. I utilise LED No. 11 (in the green sector) if a decrease, and LED No. 6 (in the amber sector) if an increase is awaited in pulsatile flow through the finger tip.

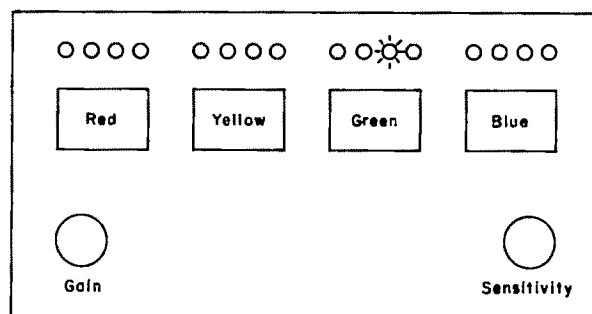


Fig. 1. Cutaneous blood flow monitor illustrating peak amplitude calibrated on to light-emitting diode No. 11 in the green sector.

The clinical value of the device lies in the format of the display. Its inspiration was derived from the article on peak pulse amplitude¹ but we have come a long way from the days of carbon microphones and ex-RAF disposal milliammeters! The physically tenuous nature of the waveform on a cathode ray oscilloscope or, for that matter, the auxiliary small-scale bar graph display on current models of oximeters, is really not of much use when one wishes to observe any tendency to change in the amplitude of pulsatile cutaneous blood flow as a significant clinical sign. The physiological significance of this sign is not clear; nevertheless there is a real place, independent of the oximeter, for a cutaneous blood flow monitor in the recovery room. If a patient is vasoconstricted despite normal blood pressure, is he/she still under sympathetic stress due to pain, cold or hypovolaemia? This form of display, which acts as an alerting device, efficiently draws attention to such possibilities. Can recovery rooms any longer be without it?

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Reference

1. BEDDARD JRJ. Amplitude observation during closed circuit halothane anaesthesia, with the vaporizer inside the circuit. *British Journal of Anaesthesia* 1965; 37: 354-62.

Book reviews

Common problems in cardiac anaesthesia	74	Muscle relaxants. Side effects and a rational approach to selection	75
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Common problems in cardiac anaesthesia

Edited by J.G. REVES AND K.D. HALL. Pp. xix + 551. Year Book Medical Publishers, Inc., 1987. £40.50.

Just occasionally there are books published about anaesthesia that break the mould of a pretence to global accuracy and favour an approach to the subject practised by the real world. This is one such offering. The last I remember, although at a slightly lower level, was *Anaesthesia for the uninterested*, in which the authors gave a witty, slightly salacious and moderately informative account of North American anaesthesia as it was in the mid seventies. Such works lack the pomposity that comes from too many hours spent in the library and too few in the operating room. There the resemblance ends.

Common problems in cardiac anaesthesia addresses 62 adverse events associated with cardiac anaesthesia and surgery in the format of case presentation, analysis of the problem, therapeutic approach to the problem and a referenced approach to the problem. Each of the 62 problems is reviewed by a different author. The volume is well edited in that a similar format is maintained in each chapter, and there is admirably little overlap between chapters. Thankfully, many of the topics discussed are neither common nor anaesthetic in origin. Nevertheless, because of the urgency or severity of the topics considered they all impinge on anaesthetic management. They range from the consequences of technical ineptitude through inevitable and accidental pharmacological interactions, to the sequelae of justifiable operations on high-risk patients.

Thirteen chapters are devoted to ischaemic heart disease, and of these several are of relevance to the patient with ischaemic heart disease who undergoes non-cardiac surgical procedures. Growth points are well covered. There is a chapter on coronary artery bypass grafting in a patient with a renal transplant, and another considers the management of combined carotid and coronary artery disease. The section on congenital heart disease is less than comprehensive, and the omission of the advantages of sustained postoperative hypocapnia in the chapter on the management of pulmonary vascular crises is surprising.

This book should be avoided by examination candidates. Some chapters are insufficiently referenced for their purpose and set out to reflect the prejudices of the authors. For those of us who practise anaesthesia in the real world it is informative, often provocative and relatively easy reading. It should be particularly valuable for anaesthetists setting out in a career in cardiac anaesthesia and for those who anaesthetise cardiac surgical patients infrequently.

C. GILBE

The anaesthesia machine

C. PETTY. Pp. 234. Churchill Livingstone, 1987. £25.00.

Convergence of design between American and British anaesthetic machines is now occurring fairly rapidly and the American origin of this work should not deter the reader in the United Kingdom. Dr Petty considers the anaesthetic machine in 12 chapters. Chapter 1 successfully condenses the history of its subject; as its first illustration it has the mercurial airholder and breathing machine from which Humphrey Davy breathed nitrous oxide, and goes on to give the classic pictures of Snow and Clover, as well as Morton's inhaler. The closed circuits of Jackson, Waters and Sword, Neu's rotameters and Morris' copper kettle vaporizer are also included. Chapter 2 is of limited value since it is devoted to a description of one type of machine, the Ohmeda Modulus II. The following eight chapters describe the components of the anaesthetic machine and include useful sections on scavenging and pollution, piping systems and ventilators for anaesthesia.

The chapter on anaesthesia systems is of particular interest. This is a subject in which considerable differences exist between America and the United Kingdom. The Mapleson systems are described briefly after an examination of the circle system. The major part of this section is then devoted to a detailed consideration of the Bain system. The author's view may be gauged from the inclusion of two quoted opinions: this system 'will play a major role in the design of future anesthesia machines' and eventually 'qualify as a universal breathing system'. The Lack system and A-D switches are not mentioned.

The chapter on compressed gases is enlivened by the use of an acronym for the Pin Index Safety System. One method of defeating this safety system is described thus: 'If more than one washer is used, the pins may not extrude out far enough to engage the valve mating holes, thus bypassing the PISS'!

Chapter 11 is of particular value: it is devoted to safety features. 'Many have expressed grave concerns about anesthesiologists who do not routinely use oxygen analysers' says Dr Petty, and buttresses this remark with no less than six references. It is hard to disagree.

The final chapter is entitled 'Risk management and quality assurance for anesthesia machines' and here the British reader does enter territory which has not yet become familiar. We learn that 'hospital risk managers have emerged as fully fledged members of the hospital administration staff'. 'The risk manager identifies potential problems that can result in lawsuit. Patients are contacted early, a dialogue is established, and hopefully a lawsuit is avoided'.

Better rapport between the physician and the patient is pinpointed as the best risk reduction strategy.

The quality assurance manager is responsible for monitoring and evaluating patient care and ensuring that anaesthetic equipment reaches and is maintained at certain minimum standards. Accreditation of the hospital is dependent on attainment of these standards.

The book is well produced with copious large line drawings and black and white photographs, and each chapter is very adequately referenced. A pleasing feature is the profusion of references to papers from British journals. Much of this book invites direct comparison with the two standard works, *Anaesthetic equipment* and *Understanding anaesthesia equipment*, both now in their second editions and both considerably bigger books. Dr Petty covers the subjects with less detail than these authors but with emphasis on principles rather than minutiae. His work can be recommended as an introductory text on the subject. Reference to the other texts may be necessary for information about specific pieces of equipment.

The convergence of design between America and Britain mentioned above is in part the result of the slow but deliberate labours of the International Standards Organization but commercial pressures have also played a part. Two of the biggest suppliers of anaesthetic equipment in North America have European roots. These firms (Ohmeda and Dräger) have provided support for the completion of this book and their products are featured as examples throughout the work. This is stated for information and not depreciation. It is to our advantage that two major companies, who are themselves very much in competition, have found it possible to combine in patronage of this useful book.

D.C. WHITE

Fluid and electrolyte management in critical care

Edited by J. ASKANAZI, P.M. STARKER AND C. WEISSMAN. Pp. xvi + 384. Butterworths, 1986. £40.00.

This book is intended to provide intensive care clinicians and other members of the intensive care unit staff, with a practical guide to the causes and management of fluid and electrolyte disturbances in acutely ill patients. In general it fulfils this objective, although it is unlikely to be widely read by non-medical personnel and I suggest that most clinicians will read only selected chapters.

The editors have managed to achieve a degree of uniformity of style and standard to produce a readable, clinically orientated text, although they could have done more to avoid the repetition of basic concepts. Inevitably much of the information presented is readily available in standard texts and one may therefore question the justification for a book devoted solely to a consideration of fluid and electrolyte disturbances in critically ill patients. Nevertheless this publication does contain a number of authoritative and informative chapters.

The first section of this book is concerned with normal physiology and here, as is the case throughout, the contributions are detailed, clearly presented and comprehensively referenced. The second part is rather clumsily entitled 'Fluid and electrolyte management of disorders and injuries: principles of diagnosis and treatment'. It contains particularly lucid chapters on the diagnosis and treatment of acid-base disturbances and on the well-worn 'crystalloid or colloid' controversy. The authors of the latter chapter are clearly strongly biased in favour of crystalloids and in some respects a more balanced analysis would have been preferable, although their case is well argued and extensively referenced. I was disappointed by the chapter on the management of fluids and electrolytes in injury and sepsis, which provided few new insights into this clinically demanding

area. The third and last section concerns fluid and electrolyte problems in relation to disorders of specific organ systems. This includes an excellent, clinically orientated discussion of the pathogenesis and management of pulmonary oedema, while other chapters deal with fluid and electrolyte disturbances as they relate to the heart, gastrointestinal tract, liver, kidney and central nervous system. It is here that the difficulties involved in isolating disorders of fluid and electrolyte homeostasis from other aspects of patient management become most obvious.

Overall the contents of this book are of a high standard and it would be a useful, but by no means essential, addition to the intensive care unit library. Individuals are likely to be reluctant to spend £40 on a book which largely duplicates information already available in more comprehensive texts.

C. J. HINDS

Muscle relaxants. Side effects and a rational approach to selection

Edited by I. AZAR. Pp. xviii + 238. Marcel Dekker, Inc., 1987. \$69.75 (USA/Canada), \$83.50 (elsewhere).

Dr Azar, not a particularly active or well-known contributor in the field of muscle relaxants (there appears to be only one, Azar I, 10-year-old case report, which is self-cited in the references), has edited this book which forms Volume 7 of a series Marcel Dekker are publishing, entitled *Clinical pharmacology*. The series itself started with an account entitled *Nicotinic acid: nutrient-cofactor-drug* and has proceeded in a pretty-much haphazard fashion.

This is a small book (on a cost per word basis it is outrageously expensive) whose scope is limited. The text is preceded by a Series introduction ('this scholarly volume ...', etc.), a Foreword ('... most important contribution ...', etc.) and an author's preface. Here it is stated to be ... 'a compilation of information on adverse and abnormal reactions to muscle relaxants.' The subtitle, *Side effects and a rational approach to selection*, seems rather to assume that a drug is chosen primarily because of its side effects.

Given this limited scope this is a reasonable account of the side effects of muscle relaxants although that strikes me as being a topic more suitable for a chapter in a book than a whole book itself. There are eight chapters: autonomic responses to muscle relaxants; histamine release by muscle relaxants; muscle relaxants in patients with neuromuscular disorders; succinylcholine-induced hyperkalaemia; malignant hyperthermia; muscle relaxants and the patient with renal and/or hepatic failure; non-depolarising muscle relaxants in burned patients; and prolonged apnoea following succinylcholine administration. They are all satisfactory little reviews by an array of contributors varying from acknowledged world authorities to British senior registrars doing their BTA (Been to America) diploma.

So this expensive little book fulfils its limited scope. This sort of thing seems to me to be publishing for publishing's own sake and I suppose if a few libraries buy it the printing costs will be covered and everyone makes a bit of money. If it's not in your own department library you will be unlikely to miss it.

R.M. JONES

Books received

Some or all of the titles listed here may be reviewed in future issues of *Anaesthesia*.

Anaesthesia and transplantation surgery.

Edited by B.R. BROWN. Pp. xiv + 257. F.A. Davis Co., 1987.

Anaesthetic literature

This section of *Anaesthetic Literature* contains references taken from *Current Contents—Life Sciences* for September 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

- Intracellular recordings from myenteric neurones in the human colon. BROOKES SJH, EWART WR, WINGATE DL. *Journal of Physiology* 1987; **390**: 305.
- Effects of adrenergic agents on colonic motility. ESSER MJ, MAHONEY JL *et al.* *Surgery* 1987; **102**: 416.
- Reversal of the effects of centrally-administered morphine on colonic motility in dogs by the benzodiazepine receptor antagonist. FIORAMONTI J, FARGAS MJ, BUENO L. *Life Sciences* 1987; **41**: 1449.
- Exogenous opiates: their local mechanisms of action in the canine small intestine and stomach. FOX JET, DANIEL EE. *American Journal of Physiology* 1987; **253**: G179.
- Plasma catecholamines following cecal ligation and puncture in the rat. KOVARIK MF, JONES SB, ROMANO FD. *Circulatory Shock* 1987; **22**: 281.
- Pathology of neuromuscular disorders of the small intestine and colon. KRISHNAMURTHY S, SCHUFFLER MD. *Gastroenterology* 1987; **93**: 610.
- Peripheral neuropathy associated with Crohn's disease. NEMNI R, FAZIO R *et al.* *Neurology* 1987; **37**: 1414.
- Ion transport in human colon *in vitro*. SELLIN JN, DE SOIGNIE R. *Gastroenterology* 1987; **93**: 441.
- Abnormal vagal function in irritable bowel syndrome. SMART HL, ATKINSON M. *Lancet* 1987; **2**: 475.

Pharmacology

Adrenergic drugs and their antagonists

- Beta blockers in combination with class 1 antiarrhythmic agents. DEEDWANIA PC, OLUKOTUN AY *et al.* *American Journal of Cardiology* 1987; **60**: 21D.
- Effects of autonomic blockade on cardiac function at rest and during upright exercise in humans. KELBAEK H, HARTLING OJ *et al.* *Journal of Applied Physiology* 1987; **63**: 554.
- Electrophysiology of beta blockers in supraventricular arrhythmias. KOWEY PR, FRIEHLING TD, MARINCHAK RA. *American Journal of Cardiology* 1987; **60**: 32D.
- The pharmacokinetics of yohimbine in man. OWEN JA, NAKATSU SL *et al.* *European Journal of Clinical Pharmacology* 1987; **32**: 577.
- Drugs with combined alpha- and beta-adrenoceptor blocking properties. RUFFOLO RR JR, NICHOLS AJ. *ISI Atlas of Science—Pharmacology* 1987; **1**: 241.
- Sotalol: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic experience to date. SINGH BN, DEEDWANIA P *et al.* *Drugs* 1987; **34**: 311.
- Electrophysiologic effects of beta blockers in ventricular arrhythmias. VENDITTI FJ JR, GARAN H, RUSKIN JN. *American Journal of Cardiology* 1987; **60**: 3D.
- Anorectic effect of ephedrine. ZARRINDAST MR, HOSSEINI-NIA T, FARNOODI F. *General Pharmacology* 1987; **18**: 559.

Anaesthetic agents

- Influence of halothane on control of breathing in intact and decerebrated cats. GAUTIER H, BONORA M, ZAOUTI D. *Journal of Applied Physiology* 1987; **63**: 546.

- The effects of general anaesthetics on GABAergic synaptic transmission. KEANE PE, BIZIERE K. *Life Sciences* 1987; **41**: 1437.
- Hormonal responses to balanced anesthesia: low-dose ketamine/neuroleptanalgesia. ROYBLAT L, LEVY J *et al.* *Current Therapeutic Research* 1987; **42**: 253.
- Evaluation of anaesthetic depth. SEBEL PS. *British Journal of Hospital Medicine* 1987; **38**: 116.

Analgesic agents

- Chemical characterization and regulation of endogenous morphine and codeine in the rat. DONNERER J, CARDINALE G *et al.* *Journal of Pharmacology and Experimental Therapeutics* 1987; **242**: 583.
- Naloxone reverses the serotonin dependent hypotensive action of CGP 6085 A. GOLDSTEIN DJ, KULAKOWSKI EC *et al.* *Life Sciences* 1987; **41**: 1369.
- Morphine reduces vagal-stimulated gastric acid secretion through a central action. HO MM, DAI S, OGLE CW. *European Journal of Pharmacology* 1987; **139**: 251.
- Effects of meperidine on oxygen consumption, carbon dioxide production and respiratory gas exchange in postanesthesia shivering. MACINTYRE PE, PAVLIN EG, DWERSTEG JF. *Anesthesia and Analgesia* 1987; **66**: 751.
- Naloxone reduces ventilatory depression of brain hypoxia. NEUBAUER JA, POSNER MA *et al.* *Journal of Applied Physiology* 1987; **63**: 699.
- Enhanced binding of morphine and nalorphine to opioid delta receptor by glucuronate and sulfate conjugations at the 6-position. OGURI K, YAMADAMORI I *et al.* *Life Sciences* 1987; **41**: 1457.
- Local and neurally mediated effects of sufentanil on canine skeletal muscle vascular resistance. O'KEEFE RJ, DOMALIKWAWRZYNSKI L *et al.* *Journal of Pharmacology and Experimental Therapeutics* 1987; **242**: 699.
- Ethanol-induced analgesia. POHORECKY LA, SHAH P. *Life Sciences* 1987; **41**: 1289.

Muscle relaxants

- Edrophonium testing for esophageal pain: concurrence and discord. CASTELL DO, RICHTER JE. *Digestive Diseases and Sciences* 1987; **32**: 897.
- Myasthenia gravis—a model disorder of acetylcholine receptors. DRACHMAN DB. In: KANDEL ER, ed. *Molecular neurobiology in neurology and psychiatry*. New York: Raven Press, 1987: 65.
- Lambert-Eaton myasthenic syndrome. I. Early morphological effects of IgG on the presynaptic membrane active zones. FUKWOKA T, ENGEL AG *et al.* *Annals of Neurology* 1987; **22**: 193.
- Lambert-Eaton myasthenic syndrome. II. Immunoelectron microscopy localization of IgG at the mouse motor end-plate. FUKWOKA T, ENGEL AG *et al.* *Annals of Neurology* 1987; **22**: 200.
- Evaluation of oral skeletal muscle relaxants in the morphine induced straub tail test in mice. PONG SF, SWEETMAN JM *et al.* *Drug Development Research* 1987; **11**: 53.
- Atropine enhances neuromuscular transmission in humans. WALI FA, BRADSHAW EG *et al.* *Fundamental and Clinical Pharmacology* 1987; **1**: 59.
- Alcuronium pharmacodynamics in dogs: effect-concentration relationships in the diaphragmatic and limb muscles. WALKER

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

JS, SHANKS CA *et al.* *Journal of Pharmacy and Pharmacology* 1987; **39**: 614.

Other drugs

Drug interaction between propafenone and metoprolol. WAGNER F, KALUSCHE D. *British Journal of Clinical Pharmacology* 1987; **24**: 213.

Complications

Optic neuropathy and amiodorone therapy. FEINER LA, YOUNGE BR *et al.* *Mayo Clinic Proceedings* 1987; **62**: 702.

Synergistic interaction between nitrogen dioxide and respirable aerosols of sulfuric acid or sodium chloride on rat lungs. LAST JA, WARREN DL. *Toxicology and Applied Pharmacology* 1987; **90**: 34.

General anaesthetic procedures

Peroperative hypothermia prevention. BERNARD JM, PINAUD M, SOURON R. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 521.

Nitrous oxide for blood pressure control after coronary artery surgery: a dose-response hemodynamic study in postoperative patients. DISESA VJ, MARK J *et al.* *Annals of Thoracic Surgery* 1987; **44**: 189.

Postoperative care and problems in liver transplantation. GRENVIK A, GORDON R. *Transplantation Proceedings* 1987; **19** (No. 4, Suppl. 3): 26.

Intensive care and intraoperative management of the brain-dead organ donor. JORDAN CA, SNYDER JV. *Transplantation Proceedings* 1987; **19** (No. 4, Suppl. 3): 21.

Update on anesthesia for adult liver transplantation. KANG Y, AGGARWAL S, FREEMAN JA. *Transplantation Proceedings* 1987; **19** (No. 4, Suppl. 3): 7.

Haemodynamic effects of prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia—studies associated with peripheral arterial surgery. MONK CR, COATES DP *et al.* *British Journal of Anaesthesia* 1987; **59**: 954.

General interest

Overlap myasthenic syndrome—combined myasthenia gravis and Eaton-Lambert syndrome. OH SJ, DWYER DS, BRADLEY RJ. *Neurology* 1987; **37**: 1411.

Local analgesia

Free-base cocaine use associated with bronchiolitis obliterans organizing pneumonia. PATAL RC, DUTTA D, SCHONFIELD SA. *Annals of Internal Medicine* 1987; **107**: 186.

Seizures after intraurethral instillation of lidocaine. SUNDARAM MBM. *Canadian Medical Association Journal* 1987; **137**: 219.

Spinal and epidural analgesia

Continuous epidural analgesia in the heparinized vascular surgical patient—a retrospective review of 912 patients. BARON HC, LARAJA RD *et al.* *Journal of Vascular Surgery* 1987; **6**: 144.

Influence of age on vascular absorption of lidocaine from the epidural space. FINUCANE BT, HAMMONDS WD, WELCH MB. *Anesthesia and Analgesia* 1987; **66**: 843.

Influence of epidural blockade on postoperative plasma fibronectin concentrations. HESSELVIK F, BRODIN B *et al.* *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47**: 435.

Effect of intrathecal bupivacaine on somatosensory evoked potentials following dermatomal stimulation. LUND C, SELMAR P *et al.* *Anesthesia and Analgesia* 1987; **66**: 809.

Sympathetic activity and haemodynamic variables during spinal analgesia in man. MALMQVIST LA, BENGTSSON M *et al.* *Acta Anaesthesiologica Scandinavica* 1987; **31**: 467.

Spinal opioids

Ventilatory response to carbon dioxide after intramuscular and epidural fentanyl. GUENERON JP, ECOFFEY C *et al.* *Anesthesia and Analgesia* 1987; **66**: 707.

Prolonged spinal analgesia in the rat with the alpha-adrenoceptor

agonist oxymetazoline. SHERMAN S, LOOMIS C *et al.* *European Journal of Pharmacology* 1987; **140**: 25.

Obstetric anaesthesia and analgesia

Epidural butorphanol or morphine for the relief of post-caesarean section pain: ventilatory responses to carbon dioxide. ABBOUD TK, MOORE M *et al.* *Anesthesia and Analgesia* 1987; **66**: 887.

Doppler assessment of umbilical artery blood flow for the prediction of outcome in fetal cardiac abnormality. AL-GAZALI W, CHAPMAN MG *et al.* *British Journal of Obstetrics and Gynaecology* 1987; **94**: 742.

Progressive resetting of sodium-renin-aldosterone relationships in human pregnancy. BROWN MA, NICHOLSON E *et al.* *Clinical and Experimental Hypertension* 1986; **5**: 349.

A prospective study investigating the mechanism of thrombocytopenia in preeclampsia. BURROWS RF, HUNTER DJS *et al.* *Obstetrics and Gynecology* 1987; **70**: 334.

Fasting hyperinsulinemic hypoglycemia after ritodrine therapy for premature labor. CALDWELL G, SCOUGALL I *et al.* *Obstetrics and Gynecology* 1987; **70**: 478.

Treatment of hypertension in pregnancy. GALLERY EDM. *ISI Atlas of Science-Pharmacology* 1987; **1**: 199.

Maternal posture in second stage and fetal acid base status. JOHNSTONE FD, ABOELMAGD MS, HAROUNY AK. *British Journal of Obstetrics and Gynaecology* 1987; **94**: 753.

A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. MABIE WC, GONZALEZ AR *et al.* *Obstetrics and Gynecology* 1987; **70**: 328.

Drugs of abuse in pregnancy—an overview. O'CONNOR MC. *Medical Journal of Australia* 1987; **147**: 180.

Technical aspects of fetal doppler measurements. RUISSE CJ, VAN VUGHT JMG *et al.* *Gynecologic and Obstetric Investigation* 1987; **24**: 1.

Preeclampsia, delivery, and the hemostatic system. SALEH AA, BOTTOMS SF *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157**: 331.

Diabetes insipidus—a postpartum complication. TULANDI T, YUSUF N, POSNER BI. *Obstetrics and Gynecology* 1987; **70**: 492.

Paediatric anaesthesia and intensive care

Central nervous system structural lesions causing apnea at birth. BRAZY JE, KINNEY HC, OAKES WJ. *Journal of Pediatrics* 1987; **111**: 163.

Cardiorespiratory function in asymptomatic survivors of neonatal respiratory distress syndrome. DRISCOLL DJ, KLEINBERG F *et al.* *Mayo Clinic Proceedings* 1987; **62**: 695.

Fetal monitoring during emergency obstetric transport. ELLIOTT JP, TRUJILLO R. *American Journal of Obstetrics and Gynecology* 1987; **157**: 245.

Continuous respiratory support in quadriplegic children by bilateral phrenic nerve stimulation. GARRIDO H, MAZAIIRA J *et al.* *Thorax* 1987; **42**: 573.

Maturation of spontaneous fetal diaphragmatic activity and fetal response to hypercapnia and hypoxemia. IOFFE S, JANSEN AH, CHERNICK V. *Journal of Applied Physiology* 1987; **63**: 609.

Modification of an infant incubator for exposure of experimental animals to nitrous oxide. LEWIS JL, PRUHS RJ, QUOCK RM. *Journal of Pharmacological Methods* 1987; **18**: 143.

Pain, anaesthesia and babies. LEADING ARTICLE. *Lancet* 1987; **2**: 543.

Intracranial pressure and its monitoring in childhood: a review. NEWTON RW. *Journal of the Royal Society of Medicine* 1987; **80**: 566.

Pulse oximeter and transcutaneous arterial oxygen measurements in neonatal and paediatric intensive care. SOUTHALL DP, BIGNALL S *et al.* *Archives of Disease in Childhood* 1987; **62**: 882.

Neonatal seizures after caesarean delivery: higher risk with labor. SPELLACY WN, PETERSON PQ *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157**: 377.

Relationship between maldistribution of ventilation and airways obstruction in children with asthma. WALL MA, MISLEY MC *et al.* *Respiration Physiology* 1987; **69**: 287.

Pulse oximetry in preterm infants. WASUNNIA A, WHITELAW G. *Archives of Disease in Childhood* 1987; **62**: 957.

Effect of bronchodilators on airway resistance in ventilator-depen-

dent neonates with chronic lung disease. WILKIE RA, BRYAN NH. *Journal of Pediatrics* 1987; **111**: 278.

Cardiovascular system

Physiology

- Atrial natriuretic peptide in spontaneous tachycardias. CROZIER IG, IKRAM H *et al. British Heart Journal* 1987; **58**: 96.
- Effect of fibronectin supplementation in endotoxic shock in the dog. HAUPTMAN JG, BEDNAR EJ *et al. Circulatory Shock* 1987; **22**: 333.
- Classification of supraventricular tachycardias. KLEIN GJ, SHARMA AD *et al. American Journal of Cardiology* 1987; **60**: 27D.
- Brachial arterial changes in response to wrist occlusion in normotensive and hypertensive men. LEVENSON J, SIMON A, PITHOIS-MERLI I. *American Journal of Physiology* 1987; **253**: H217.
- Thoracic peridural block in experimental endotoxin shock. RICHARDT G, BORNER U *et al. Circulatory Shock* 1987; **22**: 269.
- Current views on the pathophysiology and investigation of thrombotic disorders. SALEM HH, MITCHELL CA, FIRKIN BG. *American Journal of Hematology* 1987; **25**: 463.
- Effects of renal perfusion pressure on the natriuresis induced by atrial natriuretic factor. SEYMOUR AA, SMITH SG, MAZACK EK. *American Journal of Physiology* 1987; **253**: F234.
- Mechanism of histamine actions in human coronary arteries. TODA N. *Circulation Research* 1987; **61**: 280.
- Pharmacokinetics of methylprednisolone succinate, methylprednisolone and lidocaine in the normal dog and during hemorrhagic shock. TOUTAIN PL, AUTEPAGE A *et al. Journal of Pharmaceutical Sciences* 1987; **76**: 528.
- Adenosine in hemorrhagic shock: possible role in attenuating sympathetic activation. TING CS, CHU KM *et al. Life Sciences* 1987; **41**: 1375.
- Gastrointestinal plasma leakage in endotoxic shock. Inhibition by prostaglandin E2 and by a platelet-activating factor antagonist. WALLACE JL, STEEL G, WHITTLE BJR. *Canadian Journal of Physiology and Pharmacology* 1987; **65**: 1428.
- Pathophysiology of acute and chronic cardiac failure. WEBER KT, JANICKI JS *et al. American Journal of Cardiology* 1987; **60**: 3C.

Treatment and medication

- Glyceryl trinitrate (nitroglycerin) and the organic nitrates: choosing the method of administration. ABRAMS J. *Drugs* 1987; **34**: 391.
- Control of pacemaker rate by impedance-based respiratory minute ventilation. ALT E, HEINZ M *et al. Chest* 1987; **92**: 247.
- Haemodynamic effects of nitrates, with special reference to the coronary circulation. AMTORP O. *Drugs* 1987; **33** (Suppl. 4): 39.
- A controlled clinical trial of high-dose methylprednisolone in the treatment of severe sepsis and septic shock. BONE RC, FISHER CJ JR *et al. New England Journal of Medicine* 1987; **317**: 653.
- Disopyramide: a reappraisal of its pharmacodynamic and pharmacokinetic properties. BROGDEN RN, TODD PA. *Drugs* 1987; **34**: 151.
- Exercise-induced hyperkalaemia: effects of beta-adrenoceptor blocker vs diuretic. CLEROUX J, PETERSON M, LEENEN FHH. *British Journal of Clinical Pharmacology* 1987; **24**: 225.
- Pharmacology of enoximone. DAGE RC, KARIYA T *et al. American Journal of Cardiology* 1987; **60**: 10C.
- Do oxygen consumption and carbon dioxide production affect cardiac output after cardiopulmonary bypass? DAMASK MC, WEISSMANN C *et al. Archives of Surgery* 1987; **122**: 1026.
- Current management of hypertensive emergencies. GARCIA JY JR, VIDT DG. *Drugs* 1987; **34**: 263.
- Operative management of acute aortic arch dissection using profound hypothermia and circulatory arrest. GRAHAM JM, STINNETT DM. *Annals of Thoracic Surgery* 1987; **44**: 192.
- Calcium antagonists, vasoconstrictors and the peripheral circulation. HOF RP. *General Pharmacology* 1987; **18**: 459.
- Cardiac tamponade. HORGAN JH. *British Medical Journal* 1987; **295**: 563.
- Verapamil in essential hypertension: a comparison with atenolol plus hydralazine. HORVATH JS, FLETCHER PJ *et al. Clinical and Experimental Hypertension* 1987; **9**: 1185.
- Fibrinogen and risk of cardiovascular disease. KANNEL WB, WOLF PA. *Journal of the American Medical Association* 1987; **258**: 1183.

Successful extended cardiopulmonary preservation in the autoperfused working heart-lung preparation. KONTOS GJ, BORKON AM *et al. Surgery* 1987; **102**: 269.

Complications of cardiac resuscitation. KRISCHER JP, FINE EG *et al. Chest* 1987; **92**: 287.

Prediction of cardiac risk in non-cardiac surgical patients. LEADING ARTICLE. *Lancet* 1987; **2**: 433.

Misuse of intravenous verapamil in patients with ventricular tachycardia. RANKIN AC, RAE AP, COBBE SM. *Lancet* 1987; **2**: 472.

Haemodynamic effects of atenolol, labetalol, pindolol and captopril: comparison in hypertensive patients with special reference to changes in limb blood flow, heart rate and LV function. ROBERT DH, TSAO Y *et al. British Journal of Clinical Pharmacology* 1987; **24**: 163.

Hemodynamic, renal and hormonal responses to alpha-human atrial natriuretic peptide in patients with congestive heart failure. SAITO H, OGIHARA T *et al. Clinical Pharmacology and Therapeutics* 1987; **42**: 142.

Normothermic rapid volume replacement in traumatic hypovolemia: a prospective analysis using a new device. SATIANI B, FRIED SJ *et al. Archives of Surgery* 1987; **122**: 1044.

Neuro-ophthalmological complications of coronary artery bypass graft surgery. SHAW PJ, BATES D *et al. Acta Neurologica Scandinavica* 1987; **76**: 1.

Arterial and venous effects of verapamil in normal volunteers. THUILLIEZ C, DUHAZE P *et al. Fundamental and Clinical Pharmacology* 1987; **1**: 35.

Assay of a circulating sodium pump inhibitor in patients with essential hypertension and normotensive subjects. UMEDA T, NAOMI S *et al. Clinical and Experimental Hypertension* 1987; **9**: 1209.

Intramyocardial blood volume change in first moments of cardiac arrest in anesthetized goats. VERGROESEN I, NOBLE MIM, SPAAN JAE. *American Journal of Physiology* 1987; **253**: H307.

Effect of high-dose glucocorticoid therapy on mortality in patients with clinical signs of systemic sepsis. VET. ADMIN. SYSTEMIC SEPSIS CO-STUDY GROUP. *New England Journal of Medicine* 1987; **317**: 659.

Pentoxifylline improves tissue oxygenation after hemorrhagic shock. WAXMAN K, HOLNESS R *et al. Surgery* 1987; **102**: 358.

New class of antihypertensive acts by opening K⁺ channels. WESTON AH, ABBOTT A. *Trends in Pharmacological Sciences* 1987; **8**: 283.

Post-exercise hypotension: the effects of epanolol or atenolol on some hormonal and cardiovascular variables in hypertensive men. WILCOX RG, BENNETT T *et al. British Journal of Clinical Pharmacology* 1987; **24**: 151.

Respiration

Physiology

Transmission fatigue of the rabbit diaphragm. ALDRICH TK. *Respiration Physiology* 1987; **69**: 307.

Pulmonary surfactant—biochemistry, physiology and pathology. BOURBON JR, RIEUTORT M. *News in Physiological Sciences* 1987; **2**: 129.

Dyspnea. BURKI NK. *Lung* 1987; **165**: 269.

Platelet function in acute respiratory failure. CARVALHO AC, QUINN DA *et al. American Journal of Hematology* 1987; **25**: 377.

The clinical assessment of lung water. CUTILLO AG. *Chest* 1987; **92**: 319.

Acute respiratory failure induced by bleomycin and hyperoxia: pulmonary oedema, cell kinetics and morphology. GOAD MEP, TRYKA AF, WITSCHI HP. *Toxicology and Applied Pharmacology* 1987; **90**: 10.

Inspiratory and expiratory effects of nasal breathing. HAIRFIELD WM, WARREN DW *et al. Journal of Cleft Palate* 1987; **24**: 183.

Neuromuscular and mechanical responses to inspiratory resistive loading during sleep. HUDGEL DW, MULHOLLAND M, HENDRICKS C. *Journal of Applied Physiology* 1987; **63**: 603.

Pneumotaxic mechanisms influence phrenic, hypoglossal and trigeminal activities. JOHN WN. *Experimental Neurology* 1987; **97**: 301.

Anaesthesia and atelectasis—the role of V(TAB) and the chest wall. JONES JG. *British Journal of Anaesthesia* 1987; **59**: 949.

Optimum capillary number for oxygen delivery to tissue in man.

- KAMIYA A, TAKEDA S, SHIBATA M. *Bulletin of Mathematical Biology* 1987; **49**: 351.
- Mechanics of the pleural space: fundamental concepts. LAI-FOOK SJ. *Lung* 1987; **165**: 249.
- Perfluorocarbons as oxygen-transport fluids. LOWE KC. *Comparative Biochemistry and Physiology* 1987; **87**: 825.
- Breathing patterns during sleep in patients with nocturnal asthma. MORGAN AD, RHIND GB *et al.* *Thorax* 1987; **42**: 600.
- In vivo contractile properties of the fatigued diaphragm. ROAD J, VAHI R *et al.* *Journal of Applied Physiology* 1987; **63**: 471.
- Serotonin receptor blockade improves cardiac output and hypoxia in porcine ARDS. SIELAFF TD, KELLUM JM *et al.* *Journal of Surgical Research* 1987; **43**: 118.
- Whole-body oxygen consumption during liver transplantation. SVENSSON KL, SONANDER HG *et al.* *Transplantation Proceedings* 1987; **19**: 56.
- Periodic breathing and hypoxia in snorers and controls: validation of snoring history and association with blood pressure and obesity. TELAKIVI T, PARTINEN M *et al.* *Acta Neurologica Scandinavica* 1987; **76**: 69.
- Does rib cage-abdominal paradox signify respiratory muscle fatigue? TOBIN MJ, PEREZ W *et al.* *Journal of Applied Physiology* 1987; **63**: 851.
- Metabolism and turnover of lung surfactant. WRIGHT JR, CLEMENTS JA. *American Review of Respiratory Disease* 1987; **136**: 426.

Treatment and medication

- Comparison of high-frequency jet ventilation with conventional mechanical ventilation for bronchopleural fistula. BISHOP MJ, BENSON MS *et al.* *Anesthesia and Analgesia* 1987; **66**: 833.
- Oxygen conservation and oxygen-conserving devices in chronic lung disease. A review. TIEP BL, LEWIS MI. *Chest* 1987; **92**: 263.

Central nervous system

Physiology

- Reduction of cerebrospinal fluid pressure by hypocapnia: changes in cerebral blood volume, cerebrospinal fluid volume and brain tissue water and electrolytes. ARTRU AA. *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 471.
- Saturable transport of peptides across the blood-brain barrier. BANKS WA, KASTIN AJ. *Life Sciences* 1987; **41**: 1319.
- Reflex origin of Parkinsonian tremor. BURNE JA. *Experimental Neurology* 1987; **97**: 327.
- Acute cerebral ischaemia: concurrent changes in cerebral blood flow, energy metabolites, and lactate. II. Changes during ischaemia. CROCKARD HA, GADIAN DG *et al.* *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 394.
- Neuropeptides and arachidonate cascade in the central nervous system. GECSE A, MEZEI Z, TELEGDY G. In: TELEGDY G, ed. *Neuropeptides and brain function*. Basel: S. Karger, 1987: 299.
- Cerebrocortical microcirculation in different stages of hypoxic hypoxia. KOZNIWSKA E, WELLER L *et al.* *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 464.
- Hydrogen ions kill brain at concentrations reached in ischemia. KRAIG RP, PETTIO CK *et al.* *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 379.
- Sleep movements and associated autonomic nervous activities in patients with Parkinson's disease. LAIHINEN A, ALIHANKA J *et al.* *Acta Neurologica Scandinavica* 1987; **76**: 64.
- Membrane defects in paramyotonia congenita (Eulenberg). LEHMANN-HORN F, RUDEL R, RICKER K. *Muscle Nerve* 1987; **10**: 633.
- Cerebral blood volume measured with inhaled CO and positron emission tomography. MARTIN WRE, POWERS WJ, RAICHLE ME. *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 421.
- Changes in cerebral blood flow during anaesthesia and surgery in the sitting position. NELSON RJ, LOVICK AH *et al.* *Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50**: 971.
- Changes in brain blood flow and oxidative metabolism during mental activity. ROLAND PE. *News in Physiological Sciences* 1987; **2**: 120.
- Gamma-hydroxybutyrate, a possible neurotransmitter. VAYER P, MANDREL P, MAITRE M. *Life Sciences* 1987; **41**: 1547.

- Action of somatostatin on the central nervous system. VESSEI L, BALAZS M, TELEGDY G. In: TELEGDY G, ed. *Neuropeptides and brain function*. Basel: S. Karger, 1987: 36.
- Molecular neurobiology of the myelinated nerve fiber—ion-channel distributions and their implications for demyelination diseases. WAXMAN SG. In: KANDEL ER, ed. *Molecular neurobiology in neurology and psychiatry*. New York: Raven Press, 1987: 7.
- Hypoxia and monosynaptic reflexes in humans. WILLER JC, MISEROCCHI G, GAUTIER H. *Journal of Applied Physiology* 1987; **63**: 639.

Treatment and medication

- Effects of high dose methylprednisolone on delayed cerebral ischemia in patients at high risk for vasospasm after aneurysmal subarachnoid hemorrhage. CHYATTE D, FODE NC *et al.* *Neurosurgery* 1987; **21**: 157.
- Cerebral perfusion pressure: a hemodynamic mechanism of mannitol and the postmannitol hemogram. ROSNER MJ, COLEY I. *Neurosurgery* 1987; **21**: 147.
- Cerebral resuscitation: pathophysiology and therapy. WAUQUIER A, EDMONDS HL, CLINCKE GHC. *Neuroscience and Biobehavioural Reviews* 1987; **11**: 287.

Endocrine and metabolic

Physiology

- Human insulin: a review of its biological activity. Pharmacokinetics and therapeutic use. BROGDEN RN, HEEL RC. *Drugs* 1987; **34**: 350.
- Effects of renal receptor activation on neurosecretory vasopressin cells. DAY TA, CIRIELLO J. *American Journal of Physiology* 1987; **253**: R234.
- Acid-base status during and after orthotopic liver transplantation. FORTUNATO FL, KANG Y *et al.* *Transplantation Proceedings* 1987; **19**: 59.
- Head-down tilt as a physiological diuretic in normal controls and in patients with fluid-retaining states. KARNAD DR, TEMBULKAR P *et al.* *Lancet* 1987; **2**: 525.
- Action of ACTH—corticosteroid axis on the central nervous system. KOVACS GL, FEKETE M *et al.* In: TELEGDY G, ed. *Neuropeptides and brain function*. Basel: S. Karger, 1987: 79.
- Pulsatility of insulin and glucagon release—physiological significance and pharmacological implications. LEFEBVRE PJ, PAOLISSO G *et al.* *Diabetologia* 1987; **30**: 443.
- The physiology of aldosterone secretion. McDUGALL JG. *News in Physiological Sciences* 1987; **2**: 126.
- Vasopressin in end-stage renal disease: relationship to salt, catecholamines and renin activity. PAPADOLIOPOULOU-DIAMANDOPOULOU N *et al.* *Clinical and Experimental Hypertension* 1987; **9**: 1197.
- A role for insulin in the aetiology and course of hypertension? REAVEN GM, HOFFMAN BB. *Lancet* 1987; **2**: 435.
- Effects of centrally administered atrial natriuretic peptide on renal functions. SHOJI M, KIMURA T *et al.* *Acta Endocrinologica* 1987; **115**: 433.
- Insulin action—biochemical and clinical aspects. SMITH U. *Acta Medica Scandinavica* 1987; **222**: 7.

Treatment and medication

- Clinical pharmacology of torasemide, a new loop diuretic. BRATER DC, LEINFELDER J, ANDERSON SA. *Clinical Pharmacology and Therapeutics* 1987; **42**: 187.
- Aldose reductase inhibitors and diabetic complications. RASKIN P, ROSENSTOCK J. *American Journal of Medicine* 1987; **83**: 298.

Pain

Treatment and medication

- Management of injection pain in children. FOWLER-KERRY S, LANDER JR. *Pain* 1987; **30**: 169.
- Epidural ketamine for postoperative pain relief after gynecologic operations—a double-blind study and comparison with epidural morphine. KAWANA Y, SATO H *et al.* *Anesthesia and Analgesia* 1987; **66**: 735.

- Measurement of pain in children with self-reporting and behavioral assessment. MAUNUKSLA E, OLKALLA KT, KORPELA R. *Clinical Pharmacology and Therapeutics* 1987; **42**: 137.
- Comparison of intramuscular dezocine with butorphanol and placebo in chronic cancer pain: method to evaluate analgesia after both single and repeated doses. STAMBAUGH HE, McADAMS J. *Clinical Pharmacology and Therapeutics* 1987; **42**: 210.

Other

Physiology

- Measurement of upper esophageal sphincter pressure. Effect of acute emotional stress. COOK LJ, DENT J *et al. Gastroenterology* 1987; **93**: 526.

Obituaries

De Saram, Phyllis Maureen, MB, BS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist with the Central Kent Hospital Group. Qualified from London University in 1946.

Evans, Andrew Richard, MRCS, LRCP, FFARCS, formerly Consultant Anaesthetist to the East Dorset Health Authority. Qualified from the London Hospital in 1965.

Gordon, John, BA, MA, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at Rowley Bristow Orthopaedic Hospital. Qualified from Cambridge University in 1937.

Jordan-Sikorska, Zbigniewa Adriana, FFARCS, DA, formerly Consultant Anaesthetist for Selly Oak Hospital Group. Qualified in Warsaw in 1938.

Laycock, John Dixon, MB, BS, MRCS, LRCP, FFARCS, DA, formerly Senior Medical Officer for the Department of Health and Social Security. Qualified from London University in 1937.

Oliver, Frederick William, MB, ChB, FFARCS, formerly Consultant Anaesthetist for the Halifax Hospital Group. Qualified from Manchester University in 1949.

Talwalkar, Surendra C., MD, FFARCS, formerly Consultant Anaesthetist in Bombay.

Young, John Victor Innes, MB, BS, FFARCS, DA, formerly Consultant Anaesthetist to the London Hospital. Qualified from London Hospital Medical College in 1951.

International news

The Society of Anaesthetists of Hong Kong Summary of President's Report 1986–7

The main event was the 7th Asian Australasian Congress of Anaesthesiologists in September, 1986. Ten other Scientific Meetings were held. Council supports the decision to form a College of Anaesthetists. The new Constitution was adopted on 24 June, 1987.

International congress calendar

1988

- 3 January–6 February.** Marriott's Mark Resort, Vail, Colorado. *14th Annual Vail Conference in Anesthesiology.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.
- 16–23 January.** Cancun, Mexico. *Advances in Anesthesiology Symposium.*
Information: Ms Francine Kurth, Department of Anesthesiology, Mount Sinai Medical Center, 1 Gustave L. Levy Place, New York, New York 10029, USA.
- 22–23 January.** Maastricht, The Netherlands. *40th Anniversary of the Netherlands Society of Anaesthesiologists.*
Information: Dr A.E.E. Meursing, Tafelberg 88, 3328 ST Dordrecht, The Netherlands.
- 6–13 February.** Marriott's Mark Resort, Vail, Colorado. *13th Annual Vail Symposium in Intensive Care.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.
- 7–11 February.** Sheraton Waikiki Hotel, Waikiki, Hawaii. *16th Obstetric Anesthesia Conference.*
Information: Arlene Rogers, The Ohio State University, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.
- 22–25 February.** Sonesta Village Hotel, Orlando, Florida. *Symposium on the Medical Management of the Surgical Patient.*
Information: Carlita M. Kearney, Program Coordinator, Office of Continuing Education, Turner 22, 720 Rutland Avenue, Baltimore, Maryland 21205, USA.
- 3–5 March.** Munich, Federal Republic of Germany. *1st International Congress on The Immune Consequences of Trauma, Shock and Sepsis, Mechanisms and Therapeutic Approaches.*
Information: Dr Eugen Faist, LM University Munich, Department of Surgery, Klinikum Grossharden, Postfach 701260, D-8000 Munich 70, Federal Republic of Germany.
- 5–9 March.** Hotel Inter-Continental, San Diego, California. *62nd Congress of the International Anesthesia Research Society.*
Information: Dr Emerson A. Moffitt, Executive Secretary, International Anesthesia Research Society, 3645 Warrensville Center Road, Cleveland, Ohio 44122, USA.
- 12–19 March.** Doubletree Lodge, Vail, Colorado. *8th Medical Monitoring Technology Conference.*
Information: Arlene Rogers, The Ohio State University, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.
- 20–24 March.** Medunsa, South Africa. *The Annual Congress of the South African Society of Anaesthetists.*
Information: Professor J.L. Couper, Department of Anaesthesiology, P.O. Box 205, Medunsa 0204, South Africa.
- 26–27 March.** Hyderabad, India. *4th Annual Conference of the Indian Society for Study of Pain.*
Information: Dr Rupendra Lal, Organising Secretary, 3-6-23 Basir Bagh, Hyderabad 500029, India.
- 27–31 March.** The Lodge at Vail, Vail, Colorado. *15th Neonatal and Infant Respiratory Symposium.*
Information: Arlene Rogers, The Ohio State University, Department of Anesthesiology, 410 West 10th Avenue, Columbus, Ohio 43210, USA.
- 5–8 April.** Nottingham. *Junior Anaesthetists' Group Annual Meeting.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
- 23–27 April.** Miami, Florida. *Miami Comprehensive Review Course in Anesthesiology.*
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

- 25-27 April.** Intercontinental Hotel, Vienna, Austria. *1st International Symposium on Echocardiography and Doppler in Cardiac Surgery.*
Information: Werner Mohl, MD, c/o Cosmos, The Travel Agency, Kartner Ring 15, A-1015 Vienna, Austria.
- 1-6 May.** Brisbane, Australia. *Annual Scientific Meeting of the Faculty of Anaesthetists and Royal Australian College of Surgeons.*
Information: Administrative Officer, Faculty of Anaesthetists, RACS Spring Street, Melbourne 3000, Australia.
- 11-13 May.** Sydney, Australia. *5th International Dental Congress on Modern Pain Control.*
Information: Australian Convention and Travel Services (ACTS), P.O. Box 1929, Canberra, ACT 2601, Australia.
- 16-19 May.** Cancun, Mexico. *1st International Symposium of Quantitative Anaesthesia.*
Information: Dr R. Samayoa de Leon, 18 av. 'B' 0-03, Zona 15, Ciudad Guatemala CA.
- 16-20 May.** US Grant Hotel, San Diego, California. *5th International Symposium: Computing in Anesthesia and Intensive Care.*
Information: UC San Diego School of Medicine, Office of Continuing Medical Education, M-017 La Jolla, California 92093, USA.
- 22-28 May.** Washington, DC. *9th World Congress of Anesthesiology.*
Information: American Society of Anesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.
- 3-4 June.** La Villette International Conference Centre, Paris, France. *MAPAR 1988.*
Information: Secretariat, MAPAR, Department d'Anesthesiologie, Hopital de Bicetre, 78 rue du General Leclerc, F-94275, Le Kremlin-Bicetre Cedex, France.
- 14-18 June.** Baveno-Stresa, Lago Maggiore, Italy. *4th European Congress on Intensive Care Medicine.*
Information: Organizing Secretariat, MGR, Piazza S. Ambrogio 16, 20123 Milan, Italy.
- 25-29 June.** Halifax, Nova Scotia. *Canadian Anaesthetists' Society Annual Meeting.*
Information: Dr G. Houle, 187 Gerrard Street E., Toronto, Ontario, Canada M5A 2E5.
- 7-10 September.** Rome, Italy. *10th Annual Meeting of the European Academy of Anaesthesiology.*
Information: EAA Secretariat, Istituto Anestesiologia, Univ. Cattolica S. Cuore, Largo A. Gemelli 8, 00186 Rome, Italy.
- 10-14 September.** Florence, Italy. *3rd International Symposium.*
Information: Professor M. Zoppi, Cespri Fondazione Pro Juventute, Via Imprunetana 124, 500200 Monterotondo, Florence, Italy.
- 14-17 September.** Brussels, Belgium. *5th International Congress.*
Information: Professor F. Camu, AZ.VU, Laarbeeklaan 101, B-1090 Brussels, Belgium.
- 15-16 September.** Southampton. *Annual Scientific Meeting, Association of Anaesthetists of Great Britain and Ireland.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.
- 1 October.** Pavia, Italy. *National Congress, Societa Italiana di Anestesiologia e Terapia Intensiva.*
Information: Dr G. Conti, SIARITI, Universita degli Studi, La Sapienza di Roma, Viale del Policlinico, 00161 Rome, Italy.
- 8-12 October.** San Francisco, California. *Annual Meeting of the American Society of Anesthesiologists.*
Information: John W. Andes, Executive Secretary, 515 Busse Highway, Park Ridge, Illinois 60068, USA.
- 13-15 October.** Mainz, Federal Republic of Germany. *7th Annual Meeting of the European Society of Regional Anaesthesia.*
Information: Klinikum fur Anasthesiologie, Postfach 3960, Langenbeckstrasse 1, 6500 Mainz, Federal Republic of Germany.
- 23-28 October.** Rio de Janeiro, Brazil. *World Congress of Gynecology and Obstetrics.*
Information: Professor Paulo Belfort, Av. Armando Lombardi, 800/223 Barra da Tijuca, 22600 Rio de Janeiro RJ, Brazil.
- 29 October-2 November.** Ballarat, Victoria, Australia. *Annual General Meeting, Australian Society of Anaesthetists.*
Information: The Secretariat, ASA, P.O. Box 600, Edgecliff, NSW 2027, Australia.
- 6-11 November.** Pendiente, Brazil. *XXXVth Brazilian Congress of Anaesthesiology.*
Information: Soc. Brasileira Anest., Rua Prof. Alfredo Gomez 36 CEP-22251, Rio de Janeiro RJ, Brazil.
- 9-12 November.** Tauranga, New Zealand. *Conference of Anaesthetists of New Zealand.*
Information: Dr M. Hugel, Conference Secretary, Department of Anaesthetics, Tauranga Hospital, Private Bag, Tauranga, New Zealand.

1989

- 26-30 June.** Copenhagen, Denmark. *20th Scandinavian Congress.*
Information: Professor S.H. Johansen, Herlev Hospital, DK 2730 Herlev, Denmark.
- 12-16 August.** Christchurch, New Zealand. *Combined Meeting, New Zealand Society of Anaesthetists and Australian Society of Anaesthetists.*
Information: The Secretariat, ASA, P.O. Box 600, Edgecliff, NSW 2027, Australia.
- 1-4 September.** Tunisia. *3rd Pan Arab Congress on Anaesthesia and Intensive Care.*
Information: Dr Jamal Al-Shanableh, P.O. Box 15404, Marka-Amman, Jordan.
- 3-8 September.** Kyoto, Japan. *5th World Congress on Intensive and Critical Care Medicine.*
Information: The 5th World Congress on Intensive and Critical Care Medicine, c/o Japan Convention Services Inc., Nippon Press Center Building, 2-2-1 Uchisaiwai-cho, Chiyoda-ku, Tokyo 100, Japan.
- 14-15 September.** Osaka, Japan. *4th International Symposium of Endocrinology in Anaesthesia and Surgery.*
Information: Department of Anesthesiology, University of Hiro-saki, School of Medicine, 5 Zaifu-cho, Hiro-saki, Aomori-ken 036, Japan.
- 26-28 September.** Swansea. *Annual Meeting of the Association of Anaesthetists of Great Britain and Ireland.*
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

1990

- 9-15 September.** Warsaw, Poland. *VIIIth European Congress of Anaesthesiology.*
Information: The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o Polish Society of Anaesthesiology and Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

1992

- 29 March-2 April.** Atlanta, Georgia. *3rd International Symposium on the History of Anaesthesia.*
Information: R.K. Calverley, MD, Clinical Professor of Anesthesiology, Medical Center, University of California, 225 Dickinson Street, San Diego, California 92103-1990, USA.
- 14-19 June.** The Hague. *10th World Congress of Anaesthesiology.*
Information: Dr Harm Lip, Nilantweg 99, 8041 AR Zwolle, The Netherlands.



1. Membership of the Association (as at 30.7.87)

The total Membership of the Association is 5474 (5284).

Honorary	70*	(69)
Ordinary	2090	(2112)
Junior	1939	(1720)
Corresponding	34	(35)
Overseas	928	(994)
Retired	386	(321)
Senior	13	(19)
Associate	14	(14)

* This figure now includes deceased Honorary Members.
(Last year's figures in brackets).

There were 25 resignations during the year.

Deaths

Council records with regret the death of the following members:

Gergis, L. (London), Oliver, F.W. (Halifax), Todd, C. G. (Ireland), Patterson, W.J. (Sheffield), Kay, G. (Australia), Spratt, L.W. (Guildford), Smith, J. (Plymouth), Magill, Sir Ivan W. (London), El-Ghammawi, S. (Renfrew), Hammerton-Fraser, A.M. (Surrey), Roper, R.E. (Lancs.).

2. John Snow Silver Medal

Council recommended the award of the John Snow Silver Medal to Dr P.J. Helliwell, FFARCS.

3. Honorary Membership

Council recommended the following for election to Honorary Membership:

Sir Cecil Montacute Clothier, KCB, QC, Chairman, Police Complaints Authority; Professor M.H. Holmdahl, Rector, University of Uppsala; Professor K. Rawnsley, CBE, Department of Psychological Medicine, University Hospital of Wales, Cardiff.

4. Pask Certificate of Honour

Council recommended the award of the Pask Certificate to:

Dr Valerie Major, Consultant Anaesthetist, CMC Hospital, Vellore, S. India; Dr P. R. Rayner, Consultant Anaesthetist, Chesterfield; Mr L.F.G. Small, DHSS, London.

5. Annual Scientific Meeting of the Association, London, 17-19 September 1986

The Annual Scientific Meeting was held at the City University, London EC1. A full scientific and social programme had been

Association of Anaesthetists of Great Britain and Ireland

Annual Report of Council 1986-1987

organised by the local committee comprising Association Officers and London anaesthetists. There were 520 registrants. The John Snow Lecture, 'Alcohol and the Medical Profession—A Case of Dependence?', was delivered by Anthony W. Clare, Professor of Psychological Medicine, St. Bartholomew's Hospital, London.

The Annual Dinner was held at the Plaisterers' Hall. Distinguished guests included Viscount Tonypandy, who proposed the toast to the Association, and Sir Cecil Clothier, KCB, QC.

6. Annual General Meeting 1986

The Annual General Meeting was held at the City University, London, on Friday 19 September 1986. The President, Dr T.B. Boulton, was in the Chair and over 170 members were present.

Honorary Membership was conferred on Professor Sir Gordon Robson, CBE. The award of the John Snow Silver Medal to Sir Gordon Robson was received with acclamation.

Honorary Membership was also conferred on Dr O.P. Dinnick, Dr D.D.C. Howat, and on Dr C.F. Scurr, CBE, MVO, Past President of the Association.

Pask Certificates of Honour were awarded to P. Cull, Esq. (London), Dr Ruth E. Mansfield (Surrey) and to Air Commodore A.J. Merrifield, QHP (Ely). The award of a Pask Certificate to Dr S. Lipton (Liverpool) was made at the Annual Dinner of Council held on 5 December 1986, at 9 Bedford Square.

The Minutes of the Meeting have been circulated to members.

7. Linkman Conference 1986

The eleventh Annual Conference of Linkmen was held at the City University, London, on Wednesday 17 September 1986. The President, Dr T.B. Boulton was in the Chair and over 160 Linkmen attended. Linkmen received a report on 9 Bedford Square and on the success of the Appeal Fund. The subjects for discussion were smoking and anaesthesia, domiciliary visits, personal accident insurance cover, National anaesthetic adverse reaction Advisory Service, adverse drug reaction reporting, equipment procurement and maintenance, the work of the Faculty and manpower.

A detailed report of the Conference has been circulated to Linkmen and published in the April 1987 issue of *Anaesthesia*.

8. Postgraduate Study Day 1986

This meeting, held jointly with the Faculty of Anaesthetists at the Royal College of Surgeons, on 18 October 1986, was again very successful. The format was similar to previous years. Eighteen lectures were delivered in three lecture theatres enabling the 430 registrants to attend six lectures of their choice.

9. Management for Anaesthetists

A whole day symposium on this topic was held on 17 January 1987, at the Royal College of Surgeons, London. Despite appalling

weather conditions, the symposium was extremely well attended, there being some 120 registrants.

10. Annual Scientific Meeting for Junior Anaesthetists 1987

The Annual Scientific Meeting for Junior Anaesthetists was held at the Queen's University, Belfast, from 8–10 April 1987. It was organised very successfully by Dr J.P.H. Fee, Dr K.G. Lowry and Dr G.W. Black, and was attended by 160 anaesthetists in training.

The scientific programme included specific sessions devoted to trauma, unsolved problems in obstetrics, paediatric update, aspects of cardiovascular anaesthesia, current concepts and research topics in Belfast.

The Pinkerton Lecture, entitled 'A Travelling Professor', was delivered by Professor J.W. Dundee, Department of Anaesthetics, Queen's University of Belfast.

Prizes for the Registrars' papers were awarded as follows:

- 1st Prize, Dr E.A. Thornberry (*Southampton*);
- 2nd Prize, Dr S.N. Chater (*Hallifax*);
- 3rd Prize, Dr K. Milligan (*Nottingham*).

The Annual Dinner was held in the City Hall, Belfast, by kind permission of the Lord Mayor.

11. Future meetings

- 1987—Postgraduate Study Day, 17 October 1987, Joint Meeting with the Faculty of Anaesthetists, Royal College of Surgeons of England, London.
- 1988—Winter Scientific Meeting and Exhibition, 15–16 January 1988, London.
 - Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting, 5–8 April 1988, Nottingham.
 - Association Linkman Conference, 14 September 1988, Southampton.
 - Annual Scientific Meeting and Exhibition, 15–16 September 1988, Southampton.
- 1989—Joint Meeting with the Canadian Anaesthetists' Society, 9–14 June 1989, Ottawa (proposed date).
 - Association Linkman Conference, 12 September 1989, Swansea.
 - Association Scientific Meeting and Exhibition, 13–14 September 1989, Swansea.
- 1990—Linkman Conference and Annual Scientific Meeting and Exhibition, 26–28 September 1990, Manchester (proposed date).
- 1993—Joint Meeting with the Canadian Anaesthetists' Society, September 1993, Edinburgh.

Other meetings

- 1987—Faculty of Anaesthetists Symposium on Cardiopulmonary Resuscitation, 5–6 November 1987, Royal College of Surgeons of England, London.
 - Annual Meeting of the Royal College of Surgeons of England, 9 December 1987, London.
- 1988—Faculty of Anaesthetists Anniversary Forum—Intensive Care, Common Problems, 16 March 1988.
 - 9th World Congress of Anaesthesiology, 22–28 May 1988, Washington DC, USA.
 - Annual Meeting of the Royal College of Surgeons of England, 15 September 1988, Cambridge. This meeting includes a Symposium on Postoperative Care of transplant patients.
- 1990—8th European Congress of Anaesthesiology, 9–15 September 1990, Warsaw, Poland.

12. Council

During the year October 1986–September 1987 Council met on four occasions and the Advisory Committee met on five occasions. The attendance of members at Council and the Advisory Committee is shown at the end of this report, together with the membership of the various subcommittees and working parties.

Council wishes to express its appreciation of Miss Ann Muir, Administrative Secretary, Mrs Betty Tyler, her assistant, and Miss Pat Plant, Financial Assistant. During the year Mrs Catherine Goff, BOC Educational Coordinator, and Dr Audrey Eccles, ICI Archivist/Librarian, have joined the administrative secretariat.

Council also wishes to express appreciation for their work and contributions to the expansion of Association activities. Council is extremely grateful to Mr Ernest Warburton, Financial Adviser, who continues to give, on a voluntary basis, outstanding support and advice on all matters financial and legal.

Retiring from Council this year will be Dr Jean M. Horton, who completes a period of two years as Vice-President, following many valued years of service to the Association as an Elected Member of Council and as Honorary Secretary.

Three Elected Members of Council also retire after their four-year term of office, namely Professor G. Smith, Dr T.W. Ogg, and Dr W.S. Wren, all of whom have contributed greatly to the work of the Association.

Nine Bedford Square, London WC1

The year has seen intense activity at 9 Bedford Square. The programme of elegantly furnishing the House and making the public rooms functional has been completed with the aid of funds raised by the Appeal. The educational programme of seminars and workshops has gained momentum and the house has been used by many medical organisations and individuals for scientific, business and social meetings.

Without doubt, the highlight of the year and a milestone in the history of anaesthesia in this country, was the Official Opening of 9 Bedford Square as the Association's Headquarters by Her Royal Highness, The Princess Margaret, Countess of Snowdon, on Thursday 9 July 1987. The reception for this unique occasion was held in Bedford Gardens, a rare privilege, and was attended by over 500 members, distinguished guests, including anaesthetists from overseas and founder donors to the Appeal Fund both from the membership and from industry. The occasion was made more outstanding by the announcement that Her Royal Highness, The Princess Margaret, had graciously agreed to become Patron of the Association.

13. Linkman Organisation

The Linkman Organisation continues to be an important communication mechanism between Council and membership. Officers and Council place a high value on the information and opinions received from Linkmen throughout the year and at the Annual Conference. A review of the list of Linkmen has been undertaken and Linkmen are particularly requested to notify the London office of any changes.

Linkmen were requested to provide information on:

- (a) Levels of assistance for the anaesthetist.
- (b) High dependency care and to identify consultants in charge of intensive care units.

A very satisfactory response to both enquiries was received and the information gathered will be presented to Linkmen at the Linkmen Conference.

Members and Linkmen are encouraged to make the Association aware of any matter of concern or interest. A list of Linkmen is given at the end of this report.

14. Education and research

The Committee (Chairman, Professor G. Smith) met twice during the last year (5 December 1986 and 24 April 1987). In addition to the traditional work of adjudicating on research and travel grant applications, a great effort has been made to originate new scientific meetings and symposia.

Grants awarded 1986/87

Research grants. A grant of £5000 to Professor J. Norman (*Southampton*) for purchase of HPLC equipment related to the pharmacology of pancuronium and vecuronium in mechanically ventilated preterm neonates; a grant of £500 to Dr W.R. Hain (*Nottingham*) to study home ventilatory care for children.

Travel grants

Council has now approved the request by the Education and Research Committee to fund two types of grants:

- (a) *Travel grants.* These are grants of up to a maximum of £500 to permit anaesthetists to visit centres for educational purposes, but do not provide funds primarily for attending scientific meetings.
- (b) *Education awards to Third World countries.* These provide grants for up to a maximum of £1000 to assist anaesthetists to spend time working in Third World Countries where their salary may need supplementation.

Several grants have been made in the past year.

Travel grants. Dr R. Page working in Ghana, £300 to study nurse anaesthesia teaching; Dr D. Devanandan, Vellore, India, £250 to permit her to visit a number of teaching hospitals in the UK; Dr M.J. Dudley (*Bristol*), £500 to lecture and teach trainee anaesthetists in East Africa.

Educational award to Third World countries. Dr M. Carter (*Middlesex Hospital*), a grant of £1000 to take up a teaching post in the Kathmandu Children's Hospital; Dr M.J. Mowbray (*Nottingham*), a grant of £1000 to take up a post in the Tribuvan University Teaching Hospital, Kathmandu.

Association Research Fellowship. Dr Angela Cooper is now in the second year of her Fellowship undertaking a study on 'Induced hypotension during neurosurgical operations'. This is a laboratory investigation in association with Dr P.J. Morris (*Cambridge*), who holds an MRC grant to fund the recurrent costs of this activity.

Scientific meetings

The Education and Research Committee has overseen the development of a very large number of extra meetings in the last year. In addition to overseeing the scientific programme of the Annual Scientific Meeting and Meeting for Junior Anaesthetists, the Committee also has the task of drawing up the programme for the Postgraduate Study Day in association with the Faculty of Anaesthetists. New activities have included the organisation of a whole day symposium on 'Management for anaesthetists'. In addition, Council has instituted a new meeting entitled 'Winter Scientific Meeting of the Association of Anaesthetists', to be held in London on 15-16 January 1988, and a most attractive programme has been formulated.

Following the success of three pilot seminars held at 9 Bedford Square in 1986, the Committee has developed an extensive range of seminars and meetings which are encompassed under the heading 'Seminars at 9 Bedford Square'. Dr J.F. Searle has been appointed Education Secretary in charge of seminar administration and, in combination with the Chairman of the Education and Research Committee, has drawn up a programme of meetings to be held at monthly intervals during 1987-88. Substantial financial support has been obtained to support some of these meetings including a grant from Eli Lilly of £1000 for the symposium on 'Recent advances in the understanding of septic shock', and Ohmeda have sponsored some five seminars during 1987/88.

Because of the number of meetings now being organised by the Association, a Meetings Coordinator, Mrs Catherine Goff, has been endowed by BOC.

The meetings at 9 Bedford Square are of three types:

- (a) Seminars from approximately 10.30 a.m. to 4 p.m.
- (b) Lunch-time seminars commencing at 11 a.m. followed by lunch at 1 p.m.
- (c) Evening seminars commencing at 6 p.m. followed by dinner at 8 p.m.

Travenol Travelling Fellowship

The Education and Research Committee is responsible for administration of a travel grant of £2500 which is donated annually by Travenol Limited for travel within the UK or overseas, to examine any applications relating to intravenous fluid therapy, parenteral nutrition or intravenous administration of drugs, blood or blood products or filtration of such products. It remains a source of disappointment that, despite additional efforts to stimulate interest, there are only a few applications.

15. Safety Committee

Meetings of the Safety Committee (Chairman, Dr P.W. Thomp-

son) were held on 6 June 1986, 14 November 1986 and 12 June 1987. Consideration was given to a wide range of queries from members and to matters raised by members of the Committee. Particular attention has been given to the possibility of producing a British Standard and/or an International Standard for lockable connectors for breathing systems and for connectors, tubing, and inlet nozzles for oxygen masks, to the management and maintenance of anaesthetic equipment, and to explosion hazards.

The Association has continued its representation on all appropriate British and International Standards Committees and real progress has been made in this work. International agreement has at last been reached on the 22/15 mm conical fittings for use in breathing systems and the completion of the British Standard for 'Continuous flow anaesthetic machines'.

On 14 November 1986, Dr P.W. Thompson handed over the Chairmanship of the Safety Committee, which he held for eight years, to Professor A.P. Adams. Dr P.W. Thompson is continuing as the Association's Liaison Officer with BSI and ISO.

16. International Relations Committee

The International Relations Committee (Chairman, Dr M.T. Inman) has met on two occasions with representatives from the British Council, the Overseas Development Administration and other voluntary agencies working in this field. Help for developing countries continues to be coordinated by the Committee. Dr T. Jack (*Leeds*) spent two months teaching in Nepal, together with Mr M. Yates, an Equipment Maintenance Technician. Dr M. Carter and Dr M.J. Mowbray have been teaching in the Children's Hospital and the University Hospital in Kathmandu.

In Zambia (Lusaka), Dr R. Sinclair and Dr I. Wilson are both lecturers in the University Hospital. They have recently run a successful workshop on anaesthesia for local clinical officers.

In Ghana (Kumasi), Dr B. O'Donoghue and Dr R. Page are working and teaching in the University Hospital.

Dr M. Dudley has spent six months in Tanzania, and Dr P. Fenton six months in Malawi.

The WFSA Refresher Course is to be held in Nairobi in October 1987, organised by Dr R. J. Eltringham. Courses for those interested in working in developing countries are held each year in Oxford (Dr M. Dobson) and at Frenchay Hospital, Bristol (Dr J. Carter).

The Exchange Programme with East Germany (DDR) has continued with a visit from Professor G. Benad of Wilhelm Pirck University, Rostock. Dr Elizabeth G. Bradshaw (*Ealing*) is due to make a return visit.

The donation of WFSA Lecture Series to Departments of Anaesthesia in developing countries has recently been increased from ten to fifteen.

17. Editorial Board

The Editorial Board (Chairman, Dr P. J. Helliwell) met three times. Several changes occurred in the composition of the Board during the year. Dr D.J. Hatch (Council Member) had reached the end of his term of office and was replaced by Dr J. Edmonds-Seal (*Oxford*). Dr S. Silver left the employment of Academic Press and is replaced by Mr Ray Aller. Dr C.E. Blogg resigned as Assistant Editor and the Board thanked him for conscientious and devoted work. Dr A.R. Aitkenhead (*Leicester*) became Assistant Editor.

A major new initiative was planned and initiated during the year. *Anaesthesia News* was launched as a separate broadsheet in April 1987 and is distributed to all members of the Association. Dr J.N. Horton (*Cardiff*) has been appointed as an Assistant Editor in order to act as an Executive Editor for this production. The Board hopes that this will meet the criticisms of those Members of the Association who feel that the Association has not been publishing sufficient information about current events. *Anaesthesia* is primarily a scientific journal, and this will enable acceleration in publication of copy received.

18. Finance Committee

The Finance Committee (Chairman, Professor M. Rosen) met twice during the year. The Committee recognises that the increased use of 9 Bedford Square during the year had resulted in increased costs, but these had been anticipated.

The Committee reviewed subscription levels for 1988-89 and recommended full membership subscription from July 1988, should be £75 per annum, with consequential adjustments to other rates.

19. Private Practice Committee

The Private Practice Committee (Chairman, Dr M.T. Inman) met once to discuss further a document on the conduct of private practice by individuals and by groups. This document should be published in 1987, together with a revised set of guidelines for anaesthetic fees in private practice. Discussions have taken place with Provident Associations, on topics including standards of care in private hospitals, availability of a consultant anaesthetist, levels of equipment and adequate provision for postoperative pain relief.

Further seminars on the organisation of private practice in the District General Hospital have been planned for November 1987 and July 1988.

20. Junior Anaesthetists' Group

The members of the JAG Committee (Chairman, Dr G.W. Hamlin) met four times in the past year. Besides these meetings and attendance at other Committees, they have been involved in the following:

The Junior Linkman Scheme. This scheme is now fully functional. The Linkmen receive an excellent newsletter, which allows the Committee to disperse information from the Association more effectively. The Committee has also been able to help members who have made contact via the Linkmen. There were 27 members attending the Annual Linkman Meeting before the Scientific Meeting in Belfast.

The Registrar Questionnaire. This has now been completed and some of the results were presented to the Annual General Meeting. They were very well received and the results are now being forwarded to the Education and Research Committee for discussion.

Flying Squad Insurance. The Committee reported to the Anaesthetists' Subcommittee of the CCHMS about this problem and a document, to be distributed to Anaesthetic Departments, has now been prepared in conjunction with Council. This has reached the proof stage and a summary was published in *Anaesthesia News*, August 1987.

The Annual General Meeting. This was held in Belfast during the Junior Scientific Meeting. It was attended by 90 people and a wide range of topics were discussed which will be followed up by the Committee.

Changes to the Committee. There have been five resignations and five new members elected at the Annual General Meeting. Dr A.D.J. Nicholl becomes Secretary and Dr D. Paul, Linkman Coordinator/Vice-Chairman.

21. Confidential Enquiry into Peri-operative Deaths

The joint study between the Association of Anaesthetists of Great Britain and Ireland and the Association of Surgeons of Great Britain and Ireland was completed at the end of 1986 and its report is expected in 1987. The working party under the Chairmanship of Professor M.D. Vickers, met twice in the last year and at its final meeting reviewed data from the study.

The protocol for the study included plans for future studies. It is planned that a new working party consider proposals in the near future. Sources for funding are being sought.

22. Anaesthetists' Subcommittee of CCHMS

The Subcommittee has explored several avenues in endeavouring to resolve the problem of personal insurance for flying squad and major disaster incidents, which has been a cause of considerable concern for some time.

The current regulations governing death and injury benefits for medical practitioners attending flying squads and major disaster incidents are considered to be inadequate. A paper has been prepared by the Subcommittee describing the various insurance options and encouraging anaesthetic departments to initiate their own insurance policies using trust funds; the paper has been summarised and published in *Anaesthesia News*.

The question of extended training for ambulance men has been a source of interest to the Subcommittee. A Joint Consultants

Committee/DHSS Working Party is being set up to look into the matter. It is felt that anaesthetists should be sympathetic to further training of the more able and responsible ambulance men and that areas for instruction could include airway management and external cardiac massage, as well as intravenous fluids. The medico-legal aspects are being explored.

The Subcommittee has considered the implementation of 'Hospital medical staffing structure: achieving a balance' in relation to anaesthetists. The need for practitioners in the intermediate level service grade is acknowledged, but it is stressed that the numbers in the grade must be relatively evenly distributed across the appropriate specialties. The Committee recognises the need to develop and expand the Overseas Doctors Training Scheme in the specialty.

Full support has been given by the Subcommittee to the resolution of the Annual Conference of Senior Hospital Staffs 1986 promoting the case of need for an improved pay and career structure for operating department assistants. This matter has been considered by the Negotiating Subcommittee.

23. Working Parties

Specialist Anaesthetic Societies. Another successful meeting was held in November 1986, between Officers of the Association and Officers of the Specialist Anaesthetic Societies. A useful exchange of information and dates of meetings took place.

Working Party on High Dependency Care (Chairman, Dr J.F. Searle). Council set up a Working Party on High Dependency Care in November 1986, with the following terms of reference:

- To enquire into the number and value of existing high dependency units in the UK.
- To consider the clinical and economic value of such units.
- To make recommendations for future developments.

The group's first task was to produce satisfactory definitions of intensive care, high dependency care and recovery care. Having done this, a detailed questionnaire has been compiled in conjunction with the Intensive Care Advisory Group. This has been sent to all consultants in charge of intensive care units throughout the UK. This will provide detailed information about the extent and nature of high dependency care and will form the basis for the Working Party's subsequent work.

Intensive Care Advisory Group (Chairman, Professor M. Rosen). Although anaesthetists have been heavily involved in intensive care in the UK for many years, there is little recent information about how this commitment is discharged. There are many different patterns of intensive care work across the country. The contractual allowance made for this work is also very variable. Council has, therefore, set up an Advisory Group with the following terms of reference:

- To advise Council on the role of the anaesthetist in intensive care.
- To determine how well this is being achieved.
- To advise what improvements are required.

The group has worked closely with the High Dependency Care Working Party. The questionnaire which has been circulated to all consultants in intensive care will provide important information on the extent of anaesthetists' involvement in intensive care, as well as that of other specialists. The group expects to advise Council on the contractual allowance which should be made for consultant anaesthetists' intensive care duties early in 1988.

Joint Working Party with Obstetric Anaesthetists' Association on Anaesthetic Services for Smaller Obstetric Units (Chairman, Professor M. Rosen). This Working Party has met on a total of three occasions, on one occasion jointly with members of the Standing Committee of the Faculty of Anaesthetists and the Royal College of Obstetricians and Gynaecologists, and representatives from the British Paediatric Association and the British Association of Perinatal Paediatrics. A document has been drawn up entitled 'Anaesthetic services for obstetrics—a plan for the future with special reference to the smaller obstetric unit'.

The document will be published and made available to members in 1987.

Working Party on Assistance for the Anaesthetist (Chairman, Dr M.M. Burrows). Council is concerned about levels of assistance available to anaesthetists and the differing grades of staff providing this service. In addition, the status and salary of operating

department assistants (ODAs), most of whom work closely with anaesthetists, is also a matter of great concern. A Working Party has been formed to look into ways of improving levels of assistance and identifying successful systems. To this end, an enquiry was made through the Linkman organisation. The high level of response to this enquiry was very encouraging and a small number of hospitals reported to have satisfactory levels of assistance, have been visited by members of the Working Party. It is hoped that the results of this survey will help anaesthetists with unsatisfactory levels of assistance to improve this provision.

24. The Resuscitation Council UK

The Resuscitation Council (Representative, Dr P.J.F. Baskett) has been enlarged and Task Groups have been formed to discuss the following subjects, in depth: basic life support, advanced life support, paediatric life support, drowning, hypothermia, training and research. More topics are planned for the future and conclusions will be published.

The main highlight of 1986 was the publication of the book *ABC of Resuscitation* by the British Medical Journal. This publication saw the collation of much of the work of the Resuscitation Council and hinted at gaps in knowledge and areas for further study. Dr T. Evans is to be congratulated on his achievements as the Editor.

The other major event of last year was the launch of the national 'Save a Life' Campaign and most members of the Council are involved in this programme either at national or local level. The Council provided the right level of expert medical advice to the Coordinating Committee in designing and implementing the Curriculum; to the British Broadcasting Corporation and the Health Education Council in the content of educational material; and, in the form of professional support, to the Campaign briefing meetings held in locations as far apart as Belfast, Taunton and Glasgow.

The research group has been active under the Chairmanship of Dr M. Ward and has held a number of useful meetings. By now all the data from the multiple centres in the study should have been received and the tasks of analysis and inference begun. A few other research projects are planned to be conducted under the aegis of the Council, for example establishing the role of Bretylum in refractory ventricular fibrillation and evaluating the possible cerebral protective role of new calcium channel blockers.

A 19-minute videofilm has been produced with the approval of The Resuscitation Council. The film is made by the Department of Teaching Media, University of Southampton, with generous financial support from Simonsen & Weel. The film is available from Simonsen & Weel, or the Department of Teaching Media, University of Southampton, Highfield, Southampton SO9 5NH, for sale or hire.

25. The Monospecialist Committee for Anaesthesia and Reanimation

The Committee (Association Representative, Dr W.R. MacRae), President, Dr P.J.F. Baskett (Faculty Representative), has met on two occasions, November 1986, Paris and April 1987, Mainz. Significant progress has been made during the year to improve the standards and quality of anaesthetic care in the EEC.

A minimum period of five years training in anaesthesia received the support of the Committee and will now be put to the UEMS.

Attention was being given to certification in the specialty of anaesthesia, with the aim of ensuring that certification did not carry a right to work in the EEC.

Assessment of training centres throughout the EEC to ensure uniformity of standard, was under consideration.

There was now considerable support throughout the EEC for the need for a postgraduate examination in anaesthesia. The Diploma of the European Academy may be a suitable examination and the matter will be the subject of further discussion.

Composition of Council, its Subcommittees and Working Parties

Council

Four meetings held (attendance in brackets).

Officers: Professor M. Rosen, President (4); Dr T.B. Boulton, Immediate Past President (3); Dr P.J.F. Baskett, Vice-President (4); Dr Jean Horton, Vice-President (2); Dr E.B. Lewis, Vice-Presi-

dent (3); Dr M.M. Burrows, Honorary Treasurer (4); Dr W.R. MacRae, Assistant Honorary Treasurer (4); Dr P. Morris, Honorary Secretary (3); Dr M.T. Inman, Immediate Past Honorary Secretary (4); Dr J.N. Lunn, Editor (4).

Elected Members: Professor A.P. Adams (2); Dr W.L.M. Baird (4); Dr Elizabeth G. Bradshaw (2); Dr K. Budd (4); Dr J. Edmonds-Seal (4); Professor W.S. Nimmo (2); Dr T.W. Ogg (4); Dr J.F. Searle (4); Professor G. Smith (4); Dr J.A. Wildsmith (4); Dr W.S. Wren (-); Dr G.W. Hamlin (4); Dr L.G. Allan (4) (until April 1987); Dr A.D.J. Nicholl (1) (since April 1987).

Co-opted Members: Dr Aileen K. Adams; Dr P.J. Helliwell; Dr P. Keane; Air Commodore C.A.B. McLaren; Professor Sir Gordon Robson; Professor M.K. Sykes; Dr W.D. Wylie; Dr J.S.M. Zorab.

Advisory Committee

Five meetings held (attendance in brackets).

Chairman: Professor M. Rosen (5); Dr M.M. Burrows (4); Dr W.R. MacRae (4); Dr P. Morris (5); Dr M.T. Inman (5); Dr J. N. Lunn (5); Dr W.L.M. Baird (4); Dr J.F. Searle (5); Professor G. Smith (3); Dr G.W. Hamlin (5).

Editorial board

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SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294**: 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119–25.
Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN. Pathogenic properties of invading micro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10*: Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUCHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

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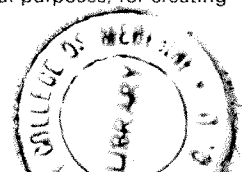
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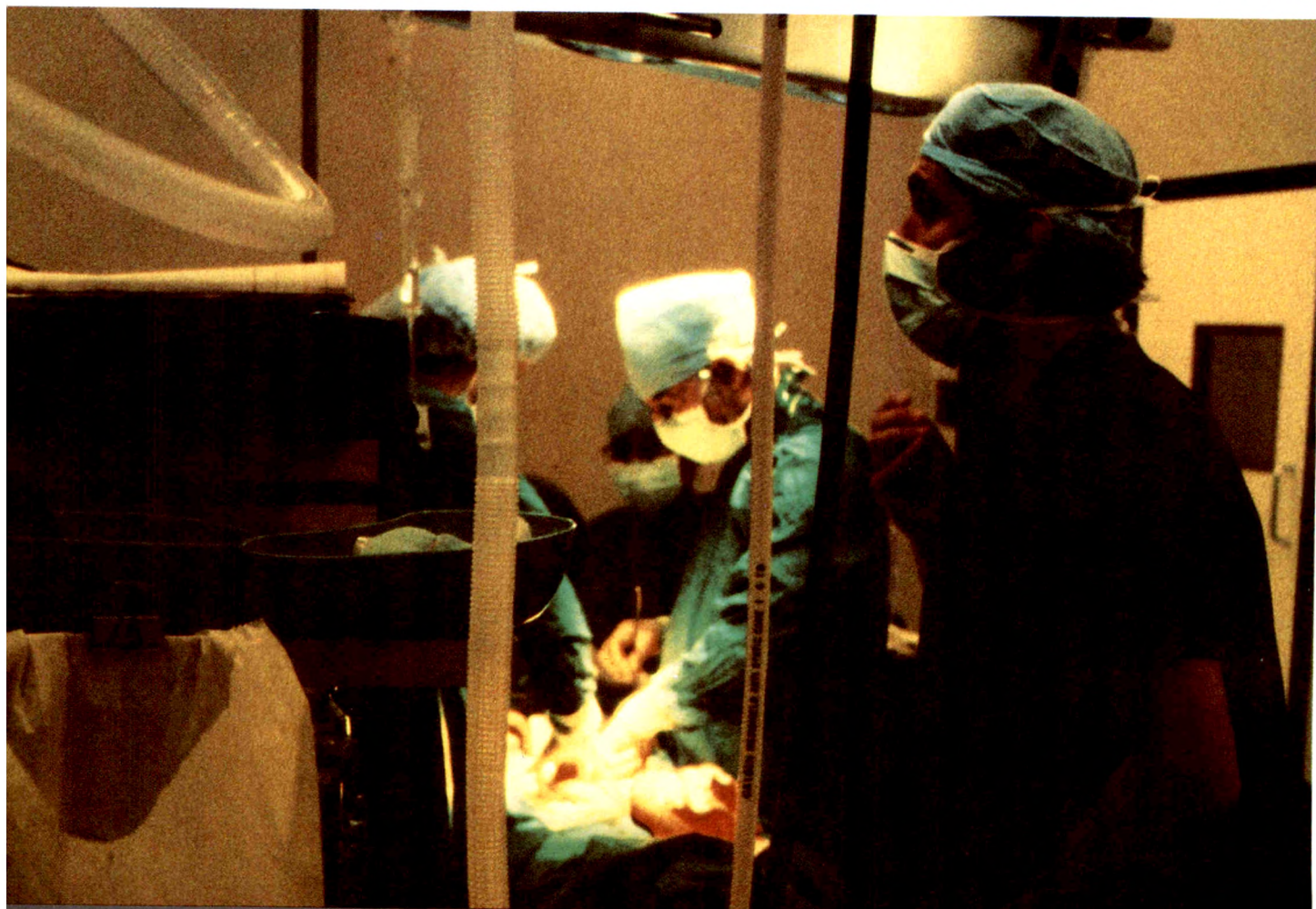
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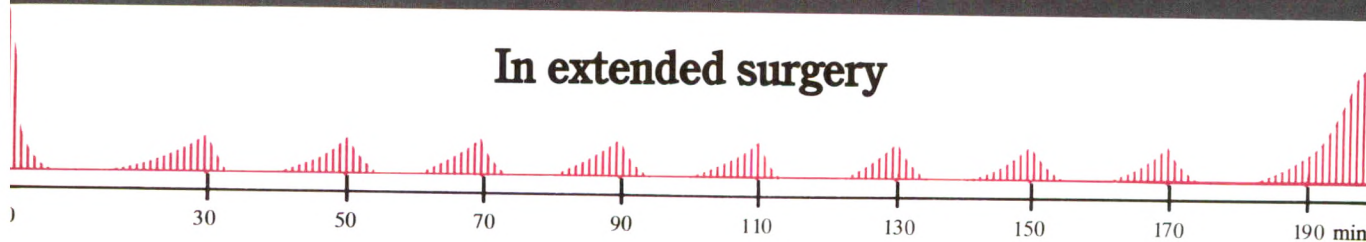
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2. Yate, P.M. *et al* (1986), *Br. J. Anaesth.*, **58**, 112 S.

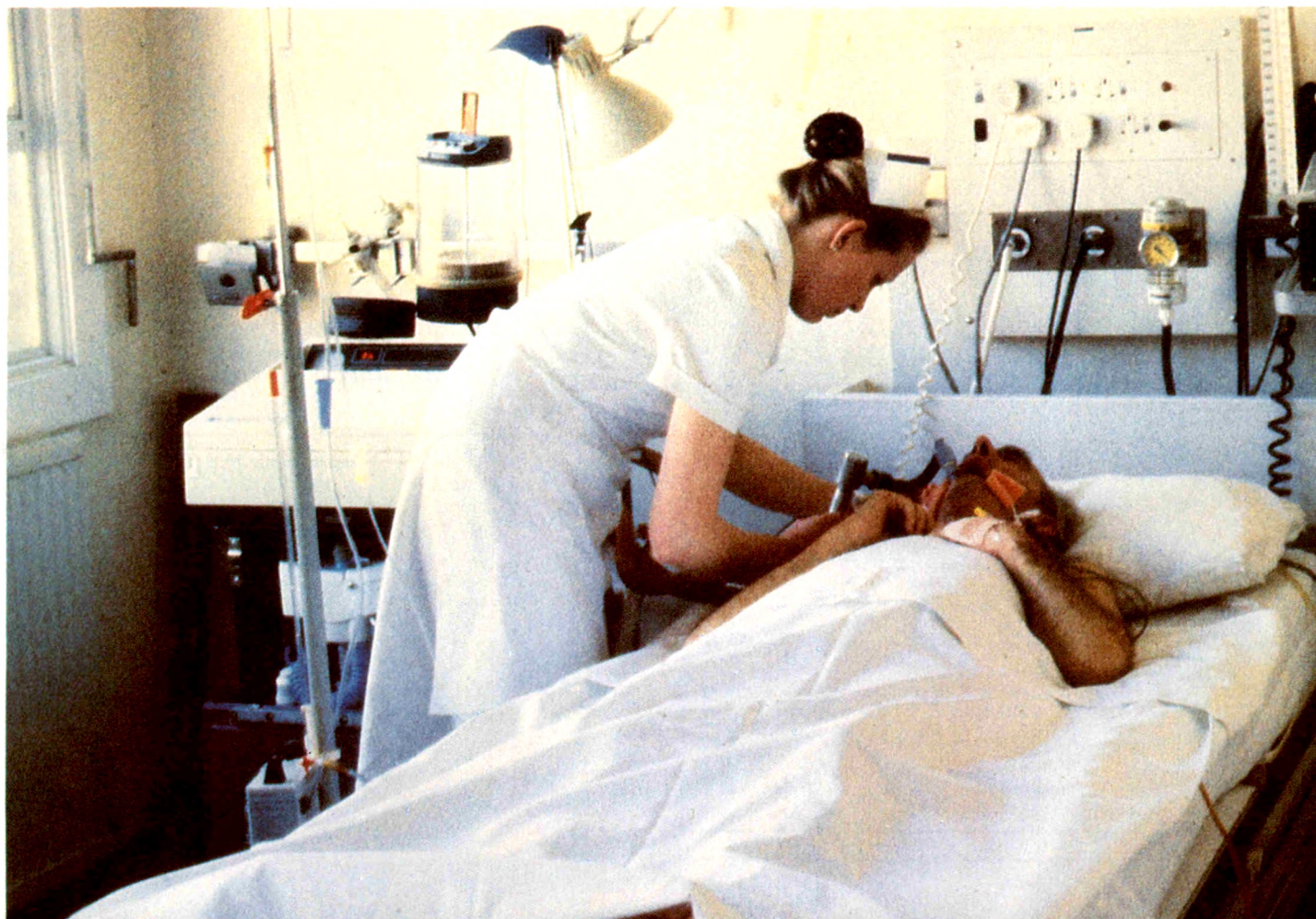
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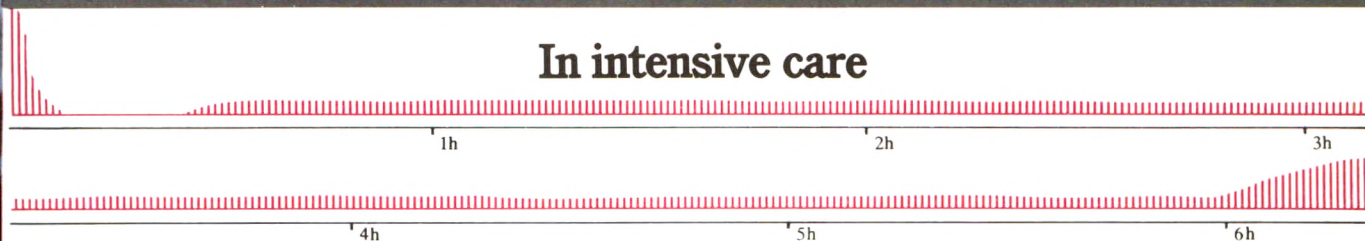


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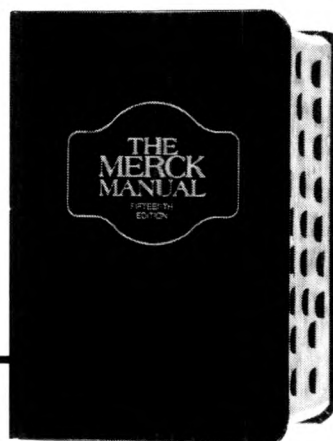
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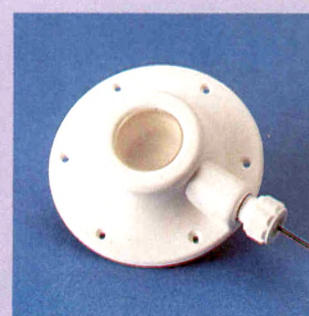
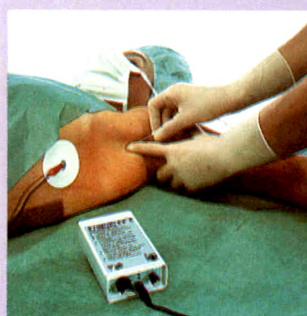
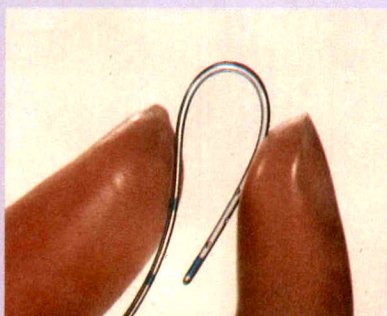
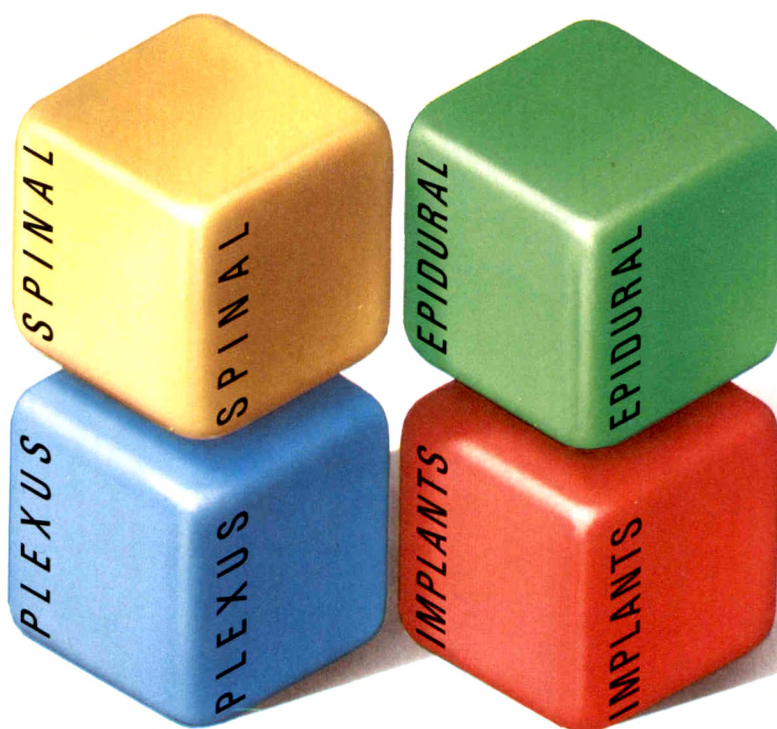
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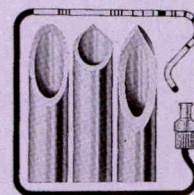
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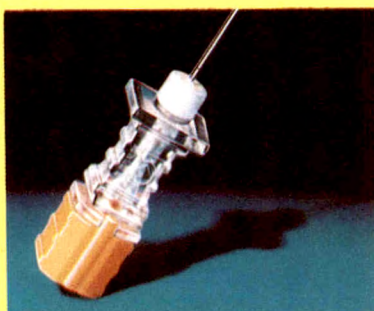
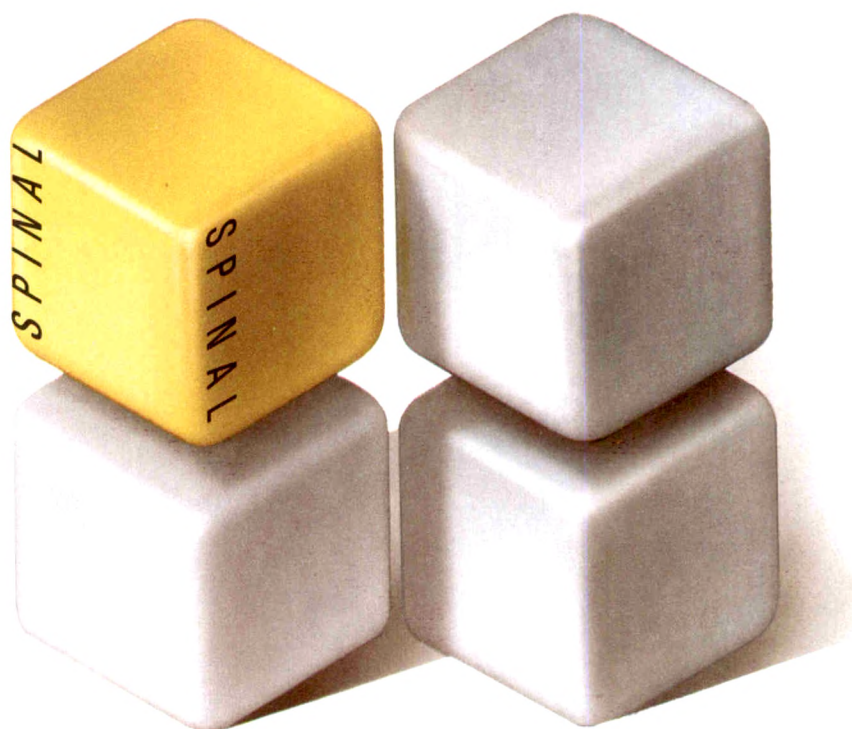
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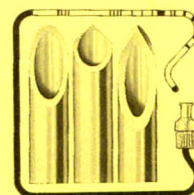
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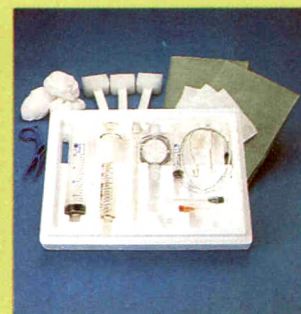
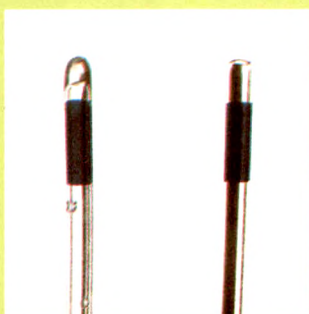
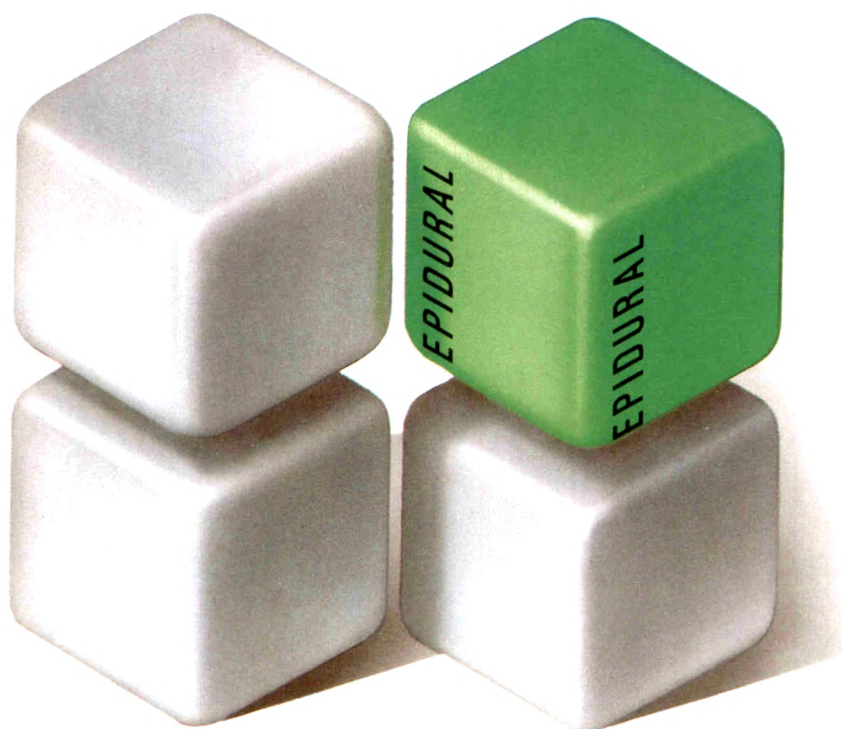
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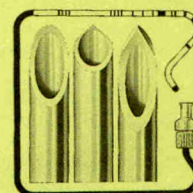


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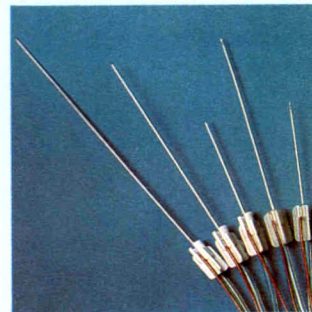
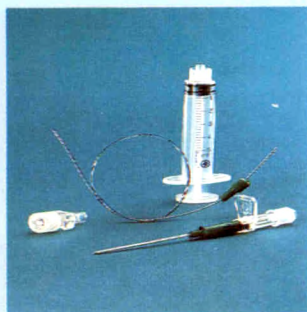
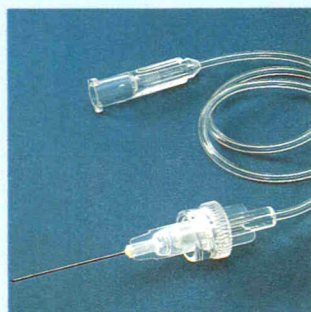
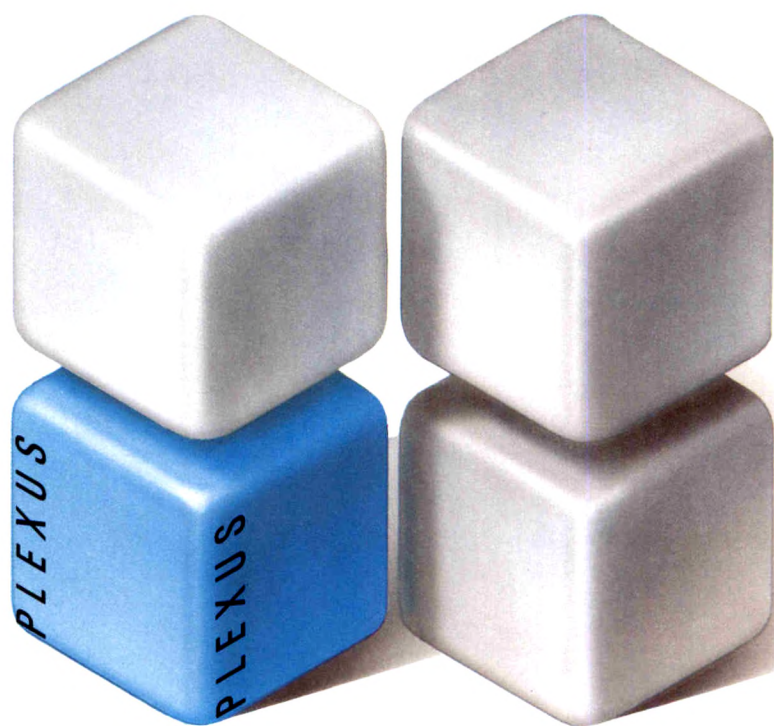
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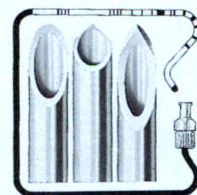


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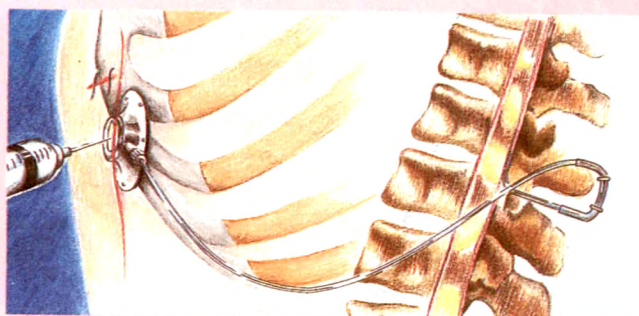
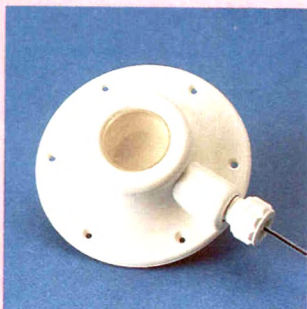
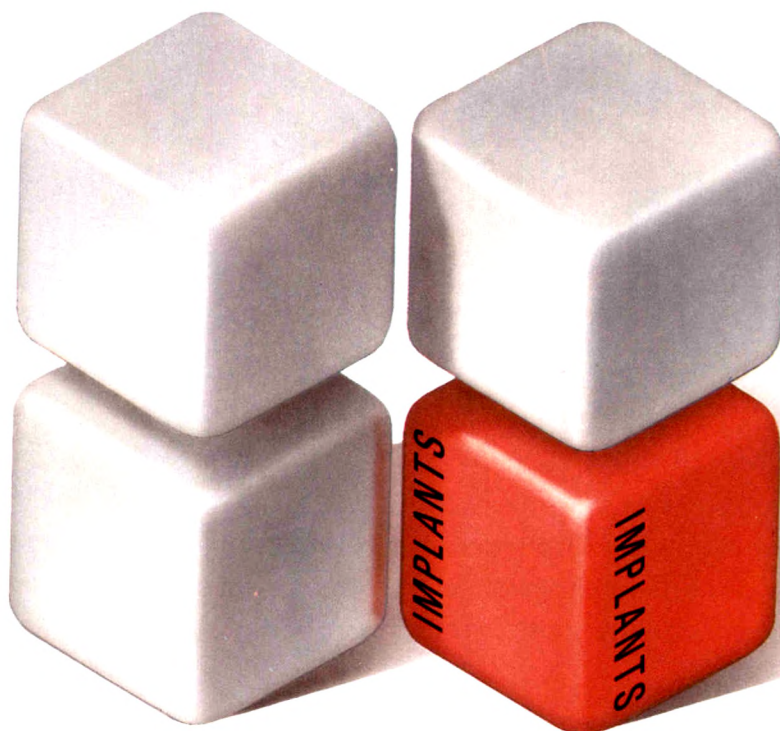
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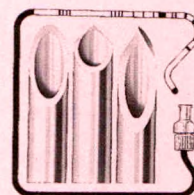


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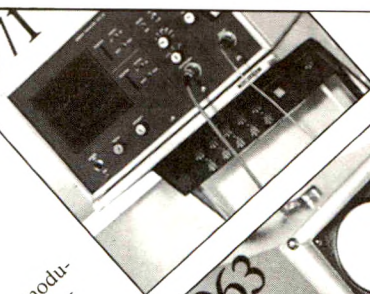


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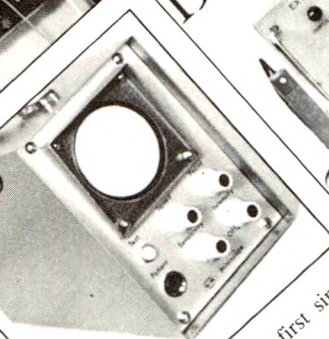
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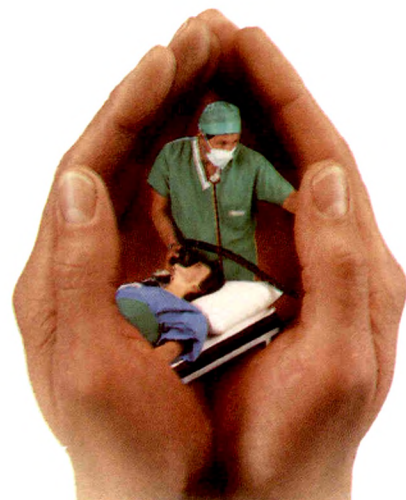
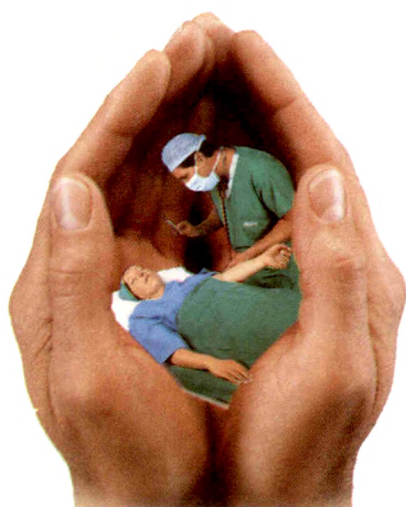
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Editorial

A confidential enquiry into peri-operative deaths

There are several definitions of audit to be found in the dictionary, but the one most suited to medical practice is 'to make an official systematic examination of . . .'. To do this on a large scale is difficult, expensive and time consuming, although 'informal audit'¹ in the form of clinicopathological conferences, case presentations and morbidity and mortality meetings are common events in most hospitals. Another type of audit is the regular inspection of hospitals by the Royal Colleges and their Faculties. It has been suggested² that these two points may explain the reluctance of medical personnel to accept large scale audit using epidemiological methods since they are already doing it themselves. Furthermore, the results of such an audit might question the entrenched attitude of consultants with regard to their clinical practice. Indeed, audit has been described as a two syllable four letter word.

There can therefore be nothing but praise for the recently published report of a Confidential Enquiry into Perioperative Deaths (CEPOD),³ which was set up under the auspices of the Associations of Anaesthetists and Surgeons of Great Britain and Ireland, with the financial backing of the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund for London. The report is both courageous and unique. Courageous because no other profession has examined the outcome of its work in this way. Unique, because although there have been three previous enquiries⁴⁻⁶ in the UK concerning anaesthetic related mortality, as well as the triennial maternal mortality reports, the present publication involves both anaesthetists *and* surgeons. To do this has required the voluntary co-operation of a large number of consultant surgeons and anaesthetists and it is gratifying that 95% of those who were approached agreed to take part in the study. Much thanks must also go to those who assessed the reports completed by the medical staff directly involved with the deceased patient.

The report concerns deaths that occurred, in 1986, within 30 days of an operation in three Regions, the Northern, South Western and North East Thames. During this time more than half a million operations were performed and 4034 deaths were reported to CEPOD. Data relating to some 70% of these deaths, a high retrieval rate which was better than expected, form the basis of the report. The overall mortality rate was 0.7%; the vast majority of these were elderly patients and death was due to progression of the surgical disease or intercurrent illness. One hundred and ninety five of these deaths were solely due to errors made in the surgical process, a rate of 0.04%. Anaesthesia, along with surgery and the patients' pathological process, was partly responsible for one death in some 1300 operations, a figure slightly worse than that published earlier.⁶ Previous reports have suggested that anaesthesia alone is responsible for one death in 10 000 operations, but the design of the current study has improved so that surgical matters are also included as factors in postoperative deaths. Thus only three deaths were solely attributable to anaesthesia, a rate of 1 in 185 000 or 0.0005%.

Several areas of substandard care have been highlighted. Junior surgeons are on occasion undertaking surgery for which they are not yet trained; supervision of juniors by consultants is often inadequate. Even consultant surgeons are operating outside their own specialist field. Unnecessary surgery is being performed on patients who have no hope of survival, and it is recommended that such decisions should only be taken at consultant or senior registrar level. There are also organisational problems. Many deaths occur in urgent and emergency cases operated on 'out of hours' perhaps because theatre space was not available during the day; it must be made available. Accidents and emergency patients are admitted at night to hospitals without full back-up facilities such as intensive care units, and who then require transfer. There must be rationalisation of services. There also appears to be a certain lack of communication between juniors and their consultants and between specialties; to operate on very sick patients requires communication between consultants. Retrieval of information was often very difficult after a patient died because notes could not be found and many forms remained unreturned owing to this problem. Unavailability of notes seriously hampers patient care and authorities must be persuaded to improve in this respect. Comments were again made on the poor standard of notes and record keeping; the advice of the defence organisations over the years continues to be ignored. The fact that the majority of deaths occurred in those aged over 70 years indicates the need for increased research and teaching into the effects of anaesthesia and surgery in this age group.

The main causes of anaesthetic concern are all too familiar. Fifteen per cent of patients were not visited pre-operatively. Availability of recovery rooms was not 100% and some were closed at night and weekends because of lack of staff. Inadequate monitoring was reported in 21% of cases. Why? Were no monitors available? Weren't they working and was the servicing and maintenance poor? Couldn't the anaesthetist be bothered to use them or possibly did not know how to use them? Interestingly, fatigue was implicated in only one death.

It is not possible here to comment on all the points raised, although some deserve comment. There seems to be a certain lack of insight amongst some of our colleagues. One surgeon judged his own performance as adequate when it was obvious that gross errors of surgical judgment had been made. It is to be hoped that the trainee anaesthetist who used the words 'No, certainly not, I am perfect' did so in a mood of flippancy. Much more sinister is the registrar who declined to complete a form 'because it is not in my job description'. Filling in forms is part of the practice of anaesthesia and general patient care and if an anaesthetist is so disinterested that he/she does not care what has happened to the patient or does not wish to know why they died so that any mistakes can be rectified, then surely they have not recognised their professional responsibility to society. It is a very sad day when a member of our profession makes such a statement.

Audit is concerned with the quality of care and its main aim should be to improve the effectiveness and efficiency of patient care. To look at one's own practice is a most difficult thing to do, but it is important that we do this ourselves, otherwise it will be forced upon us by outsiders. The public also has an interest in quality of care and they should be reassured that we are looking at our practice to identify areas where improvements can be made. For it is the purpose of audit not merely to identify poor practice but also to ensure that re-observations are made to confirm that the desired improvements have taken place. It is encouraging to know that the Royal College of Surgeons are to implement the recommendations of the CEPOD report where practicable.

This report must be regarded as a *start* only. Anaesthetists are becoming old hands at this type of epidemiological investigation, but it is gratifying that we have now been joined by surgeons, and it is to their credit they have done so. It is also encouraging to know that a nationwide study along these lines is to be started in the near future. The results of the present enquiry is essential reading for all involved in the surgical care of patients. The enormous amount of work involved in designing and collating the information generated will also then become obvious. Thus the greatest credit must go to Messrs. Buck, Devlin and Lunn who compiled and composed this report, the writing of which was not in their job descriptions either.

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M. MORGAN
Assistant Editor

References

1. MCCOLL I. Medical audit in British hospital practice. *British Journal of Hospital Medicine*. 1979; **22**: 485-9.
2. DAVIES DM. Comment on quality assurance in clinical practice in the UK: medical audit and quality control in medicine in the USA. In: LUNN JN, ed: *Quality of care in anaesthetic practice*. London: The MacMillan Press Ltd, 1984: 51.
3. BUCK N, DEVLIN HB, LUNN, JN. *The report of a confidential enquiry into perioperative deaths*. London: The Nuffield Provincial Hospital Trust and the King's Fund, 1987.
4. EDWARDS G, MORTON HJV, PASK EA, WYLIE WD. Deaths associated with anaesthesia. A report on 1000 cases. *Anaesthesia* 1956; **11**: 194-220.
5. DINNICK OP. Deaths associated with anaesthesia. Observation on 600 cases. *Anaesthesia* 1964; 536-556.
6. LUNN JN, MUSHIN WW. *Mortality associated with anaesthesia*. London: Nuffield Provincial Hospitals Trust, 1982.

Editorial notices

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979; **1**: 432-5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

H₂ antagonists and bupivacaine clearance

G. M. O'SULLIVAN, M. SMITH, B. MORGAN, D. BRIGHOUSE AND
F. REYNOLDS

Summary

The effect of the H₂ receptor antagonists cimetidine and ranitidine on bupivacaine clearance was assessed in women scheduled to undergo elective Caesarean section under epidural anaesthesia. Thirty-six women were randomly allocated to receive either no medication, cimetidine 400 mg or ranitidine 150 mg on the night prior to and on the morning of surgery. No significant difference was found between the peak bupivacaine levels: the mean (SD) values were 0.74 (0.17) µg/ml, 0.81 (0.38) µg/ml and 0.70 (0.24) µg/ml in the control, cimetidine and ranitidine groups, respectively. Similarly, the H₂ receptor antagonists did not alter the plasma bupivacaine against time curves, half-life or bupivacaine clearance in the three groups studied.

Key words

Histamine; H₂ receptor antagonists, cimetidine, ranitidine.
Anaesthetics, local; bupivacaine.

The H₂ receptor antagonist cimetidine has been shown to decrease the clearance of a number of drugs, including local anaesthetics^{1,2} and diazepam,³ because it inhibits hepatic microsomal enzymes and reduces liver blood flow.⁴ Ranitidine, like all H₂ receptor antagonists, reduces liver blood flow but has only a minimal effect on hepatic enzyme systems and has thus been implicated in fewer drug reactions than cimetidine.^{5,6} Both cimetidine and ranitidine are used as prophylaxis against acid pulmonary aspiration, whilst the amide local anaesthetic bupivacaine is widely used to provide analgesia during labour and anaesthesia for Caesarean section. Satisfactory anaesthesia for epidural Caesarean section frequently requires large volumes of bupivacaine which can, in certain circumstances, result in plasma levels within the toxic range.⁷ Thus, any interference in the clearance of bupivacaine could be of clinical importance.

This study assessed the effect of cimetidine and ranitidine on the clearance of bupivacaine in women who presented for elective Caesarean section.

Methods

Thirty-six women who required elective Caesarean section and requested epidural anaesthesia were studied in this ethically approved trial. The women received no concurrent

medication other than iron therapy, and the main indication for Caesarean section was cephalopelvic disproportion. The subjects were randomly allocated to receive either no medication ($n = 10$), cimetidine 400 mg ($n = 14$) or ranitidine 150 mg ($n = 12$) on the night prior to and on the morning of surgery. Intravenous cannulae, one for intravenous hydration and the other for blood sampling, were placed in both forearms 2–3 hours after the morning medication. A catheter was placed in the epidural space at either the L₂–L₃ or L₃–L₄ interspace following local infiltration of the skin with 1% lignocaine. After a 2 ml test dose, sufficient 0.5% plain bupivacaine was given to achieve effective blockade for Caesarean section. The circulation was preloaded with 1000 ml Hartmann's solution during performance of the block and a further 1000 ml were given prior to and during surgery. The arterial blood pressure was measured at 5-minute intervals until the delivery of the baby and thereafter at 15-minute intervals. Hypotension was treated with intravenous ephedrine when necessary. Oxygen 4 litres/minute was administered through an MC mask until delivery. The electrocardiogram was monitored throughout the procedure. Syntocinon 10 units was given after delivery of the infant. Postoperatively the mothers received epidural diamorphine 5 mg for the relief of pain.

Blood samples (5 ml) were taken for plasma bupivacaine levels at 15, 30, 60, 120, 240, 360, 480 minutes and 24 hours

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Table 1. Mean (SD) age, weight and dose of bupivacaine in the control, cimetidine and ranitidine groups. Differences between the groups were not statistically significant.

	Control (n = 10)	Cimetidine (n = 14)	Ranitidine (n = 12)
Age, years	29.6 (6.0)	30.6 (6.0)	31.8 (6.3)
Weight, kg	72.4 (3.7)	76.6 (9.3)	74.6 (10.5)
Total bupivacaine, mg	115.5 (23.5)	116.4 (18.8)	113.3 (14.8)

Table 2. Pharmacokinetic data. Differences between the groups were not statistically significant. Values expressed as mean (SD).

	Control	Cimetidine	Ranitidine
Peak level, µg/ml	0.74 (0.17)	0.81 (0.38)	0.70 (0.24)
AUC, µg hour/ml	5.32 (2.2)	5.87 (2.1)	5.11 (3.2)
<i>t</i> _{1/2} , hours	6.2 (3.0)	6.9 (2.9)	6.5 (4.8)
Clearance, ml/hour	390.1 (122.1)	404.8 (147.3)	468.9 (218.5)

after the first dose of bupivacaine. The samples were centrifuged and the plasma separated and frozen at -20°C until assayed. Plasma bupivacaine levels were measured by gas-liquid chromatography with nitrogen detection and ethyl bupivacaine as internal standard. The area under the plasma concentration against time curve (AUC) was calculated by the trapezoidal rule and extrapolated to infinity, while the half-life (*t*_{1/2}) was measured from the plasma concentration against time curve. Clearance (Cl) was calculated using the equation $Cl = D/AUC$, where D is the total dose of bupivacaine and AUC the area under the curve. Values are quoted as mean (SD). Statistical analysis was with Student's *t*-test and *p* < 0.05 was regarded as statistically significant.

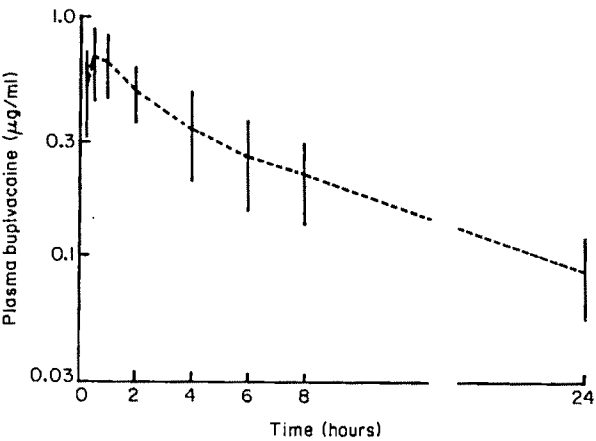


Fig. 1. Mean plasma bupivacaine concentrations in control group.

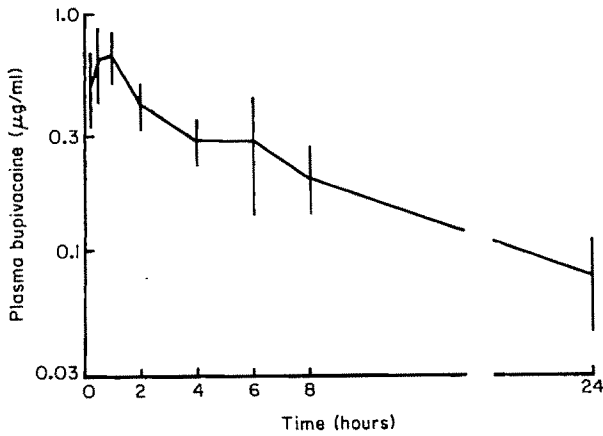


Fig. 2. Mean plasma bupivacaine concentrations in mothers who received cimetidine.

Results

Age, weight and mean dose of bupivacaine were similar in the three groups (Table 1). Plasma concentration curves during the 24-hour study period are shown in Figs. 1-4 and there was no significant difference in the plasma bupivacaine levels among the three groups. There was also no significant difference in the peak bupivacaine levels; the mean (SD) respective peak levels were 0.74 (0.17) µg/ml, 0.81 (0.38) µg/ml and 0.70 (0.24) µg/ml in the control, cimetidine and ranitidine groups. Half-life, clearance and area under the plasma concentration against time curves were also similar in the three groups (Table 2). Seven patients were given intravenous ephedrine. Apgar scores varied between 6 and 9 at 1 minute and between 7 and 10 at 5 minutes.

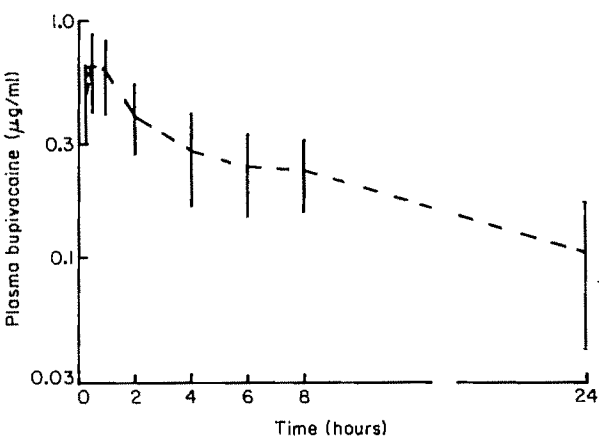


Fig. 3. Mean plasma bupivacaine concentrations in mothers who received ranitidine.

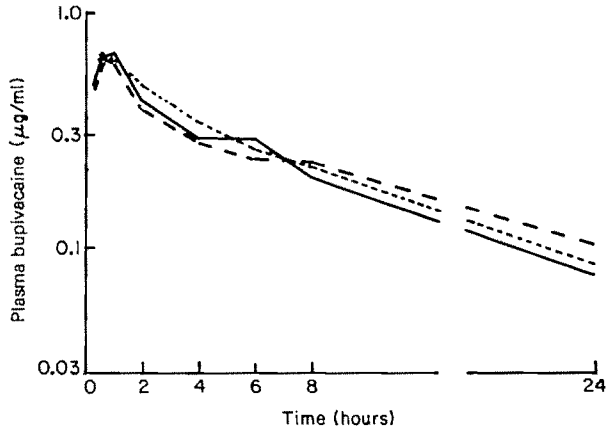


Fig. 4. Combined data.

Discussion

The H₂ receptor antagonist cimetidine, an imidazole derivative, has been shown to inhibit the metabolism of a number of drugs, including warfarin⁸ and diazepam.³ This is due to the binding of cimetidine to microsomal cytochrome P450 with a consequent decrease in oxidative metabolism. The overall effect of cimetidine is more complex since it also decreases liver blood flow and, hence, has an additional effect on those drugs such as lignocaine and propranolol which have a high hepatic clearance.⁴ An alteration of the volume of drug distribution has also been implicated in the effect of cimetidine on lignocaine disposition.¹ The furan derivative ranitidine does not bind significantly to cytochrome P450 but has a similar effect to cimetidine on liver blood flow and so appears to cause fewer drug interactions.

This study indicates that neither cimetidine nor ranitidine inhibits the clearance of bupivacaine 0.5%. The values for $t_{1/2}$ in this study are longer than those seen after intravenous administration but this probably reflects a slower rate of absorption of bupivacaine from the epidural space. The lack of effect of the H₂ receptor antagonists on bupivacaine clearance is consistent with the pharmacological properties of bupivacaine, which is highly protein bound, slowly absorbed from the epidural space and has a low hepatic extraction ratio (0.39 compared to 0.63 for lignocaine).⁹ Therefore, any change in liver blood flow caused by the H₂ receptor antagonists is less likely to affect bupivacaine clearance. Propranolol, which reduces the clearance of several drugs by both reduction of liver blood flow and depression of hepatic metabolism, has been shown to reduce systemic bupivacaine clearance.¹⁰ This effect must therefore be due to an inhibition in hepatic metabolism, since bupivacaine clearance is relatively unaffected by changes in liver blood flow.

These results are in contrast to the well documented effect of cimetidine on lignocaine clearance, in which even single pre-operative doses have been shown to reduce clearance.¹¹ In general, it appears that ranitidine does not affect lignocaine disposition.^{11,12} However, in one study by Robson *et al.*¹³ ranitidine caused a 9% reduction in systemic lignocaine clearance but no change in oral lignocaine clearance, which indicates an effect on hepatic blood flow rather than hepatic metabolism. Different study designs, in particular a longer period of ranitidine pre-treatment, probably caused this observed difference. Bupivacaine clearance might have been reduced in the present study if

the pre-operative pretreatment with the H₂ antagonists had been more prolonged or if larger doses of the drugs had been used.

Therefore, pre-operative administration of the H₂ antagonists cimetidine and ranitidine, as commonly prescribed for prophylaxis against acid aspiration, does not decrease bupivacaine clearance and these agents are not contraindicated prior to regional anaesthesia.

References

1. FEELY J, WILKINSON GR, McALLISTER CB, WOOD AJJ. Increased toxicity and reduced clearance of lidocaine by cimetidine. *Annals of Internal Medicine* 1982; **96**: 592-4.
2. KNAPP AB, MAGUIRE W, KEREN G, KARMEN A, LEVITT B, MIURA DS, SOMBERG JC. The cimetidine-lidocaine interaction. *Annals of Internal Medicine* 1983; **98**: 174-7.
3. KLOTZ U, REIMANN I. Delayed clearance of diazepam due to cimetidine. *New England Journal of Medicine* 1980; **302**: 1012-4.
4. FEELY J, WILKINSON GR, WOOD AJJ. Reduction of liver blood flow and propranolol metabolism by cimetidine. *New England Journal of Medicine* 1981; **304**: 692-5.
5. ABERNETHY DR, GREENBLATT DJ, ESHELMAN FN, SHADER RI. Ranitidine does not impair oxidative or conjugative metabolism: noninteraction with antipyrine, diazepam, and lorazepam. *Clinical Pharmacology and Therapeutics* 1984; **35**: 188-92.
6. REIMANN IW, KLOTZ U, EROLICH JC. Effects of cimetidine and ranitidine on steady-state propranolol kinetics and dynamics. *Clinical Pharmacology and Therapeutics* 1982; **32**: 749-57.
7. THOMPSON EM, WILSON CM, MOORE J, MCCLEAN E. Plasma bupivacaine levels associated with extradural anaesthesia for Caesarean section. *Anaesthesia* 1985; **40**: 427-32.
8. SERLIN MJ, SIBBON RG, MOSSMAN S, BRECKENRIDGE AM, WILLIAMS JRB, ATWOOD JL, WILLOUGHBY JMT. Cimetidine: interaction with oral anticoagulants in man. *Lancet* 1979; **2**: 317-9.
9. COUSINS MJ. Epidural neural blockade. In: COUSINS MJ, BRINENBAUGH PO, eds. *Neural blockade in clinical anaesthesia and management of pain*. Philadelphia: J.B. Lippincott, 1980: 176-274.
10. BOWDLE TA, FREUND PR, SLATTERY JT. Propranolol reduces bupivacaine clearance. *Anesthesiology* 1987; **66**: 36-8.
11. DAILEY PA, HUGHES SC, ROSEN MA, HEALY K, CHEEK DBC, PYTKA S, FISHER DM, SHNIDER SM. Lidocaine levels during Cesarean section after pretreatment with ranitidine or cimetidine. *Anesthesiology* 1985; **63**: A444.
12. FEELY J, GUY E. Lack of effect of ranitidine on the disposition of lignocaine. *British Journal of Clinical Pharmacology* 1983; **15**: 378-9.
13. ROBSON RA, WING LMH, MINERS JO, LILLYWHITE KJ, BIRKETT DJ. The effect of ranitidine on the disposition of lignocaine. *British Journal of Clinical Pharmacology* 1985; **20**: 170-3.

Subarachnoid anaesthesia for elective Caesarean section

A comparison of two hyperbaric solutions

A. R. MICHIE, R. M. FREEMAN, D. A. DUTTON AND H. B. HOWIE

Summary

Forty patients who underwent elective lower segment Caesarean section under subarachnoid anaesthesia received either 2.0 ml 0.5% cinchocaine in 6% dextrose or 2.5 ml 0.5% bupivacaine in 8% dextrose via a 26-gauge needle with the patient in the left lateral position. Onset time was rapid in both groups and the distribution of maximum ascent of sensory analgesia was T₁–T₆. Efficacy of analgesia was greater in the bupivacaine group, although the duration of both sensory and motor blockade was shorter than following cinchocaine. There were no significant differences between the two groups either in the incidence and severity of complications or in the condition of the neonates. The high incidence (50–65%) and often profound extent of hypotension seen throughout the trial, confirm the ineffectiveness of crystalloid preload of 1500 ml as a single prophylaxis against hypotension.

Key words

Anaesthesia; obstetric.

Anaesthetic techniques, regional; spinal.

The use of extradural analgesia in operative obstetrics has been investigated and refined in recent years so that it has become an established, safe and generally reliable method to provide anaesthesia for lower segment Caesarean section. The use of a two-stage top-up technique¹ has been particularly effective in achieving adequate analgesia without blockade that extends to cervical segments. Subarachnoid anaesthesia is less well established in this area and the use of an isobaric agent, such as 0.5% bupivacaine plain solution, has been shown to be unreliable and to produce occasional high blocks.^{2–4} The aim of this study was to identify a technique of subarachnoid anaesthesia that would produce adequate analgesia for a sufficient duration of time but without dangerously high blockade. The volumes chosen of the respective agents were based on our previous clinical experience.

Methods

Mothers admitted to the study were those who had requested regional analgesia for their elective Caesarean section and had given consent for spinal anaesthesia. They were randomly allocated to two groups: 20 received 2.0 ml 0.5% cinchocaine in 6% dextrose, and 20 received 2.5 ml 0.5% bupivacaine in 8% dextrose.

Technique

In all mothers the circulation was preloaded with 1.5 litres Hartmann's solution given over 20–30 minutes before injection of local anaesthetic. Lumbar puncture was performed at the level of the L_{2/3} interspace, using a 26-gauge spinal needle with the mother on the operating table in the left lateral position. L_{1/2} or L_{3/4} were used only if lumbar puncture was not possible at L_{2/3}. The predetermined volume of local anaesthetic was then injected over 20–30 seconds without barbotage, and the mother immediately returned to the supine position with left lateral tilt to avoid aortocaval compression. The mother's head was rested on two pillows, primarily for comfort but also to limit the ascent of blockade. Oxygen was given at a rate of 4–5 litres/minute until delivery of the infants. Intravenous ephedrine was given in 3–6-mg increments if hypotension less than 90 mmHg systolic occurred.

Observations

Observations were made on a double-blind basis in that the assessor had no knowledge of the agent or volume used. Arterial blood pressure and heart rate were recorded at one-minute intervals for 5 minutes and thereafter every 5

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minutes, using an automated, noninvasive device (Critikon-Dinamap 845). Cutaneous analgesia levels were determined by pinprick at 5-minute intervals. The time was noted from injection of local anaesthetic to the analgesic level reaching T_6 bilaterally, and this was defined as the onset time. Duration of sensory blockade was recorded by noting when postoperative pain was first experienced. Similarly, for motor blockade, the times were recorded at which patients could move their toes and, secondly, raise an extended leg through 30° .

The condition of the neonates was assessed by Apgar scores at one and 5 minutes, by time to establish sustained respiration and by acid-base sampling of cord blood at birth.

The incidence and frequency of complications was noted, and the efficacy of sensory blockade was recorded by placing patients in one of five categories: category A, no discomfort at all during the procedure; category B, mild discomfort but did not require systemic analgesia; category C, pain that required additional analgesia; categories D and E, required general anaesthesia after or before commencement of surgery, respectively.

Statistics

Results were analysed using Student's *t*-test, the Chi-squared test with Yate's correction and the Mann-Whitney *U* test, as appropriate.

Results

Details of the mean ages, weights and heights of the patients studied are shown in Table 1. There were no statistical differences between the groups.

Table 1. Patient data. Values expressed as mean (range).

	Cinchocaine	Bupivacaine	
Age, years	29 (23-43)	28 (17-43)	NS
Weight, kg	73.7 (54-98)	73.8 (58-101)	NS
Height, cm	158 (148-165)	157 (146-170)	NS

NS, not significant.

Onset of blockade took less than 10 minutes (mean) in both groups and was significantly shorter following bupivacaine (Table 2). Surgery was allowed to proceed only when the level of sensory analgesia was at, or above the 6th thoracic dermatome (T_6) bilaterally, and the maximum ascent of sensory blockade was in the range T_1 - T_6 in all but one patient, in the cinchocaine group (T_{11}). In addition, in these mothers the level of sensory blockade did not fall below T_6 by the end of surgery. The mean duration of both sensory and motor blockade was more prolonged in the cinchocaine group, and this was statistically significant (Table 2).

Table 2. Comparison of times of onset and durations of subarachnoid blockade. Values expressed as mean (SD).

	Cinchocaine	Bupivacaine
Onset, minutes	8.95 (4.74)	6.65* (2.83)
Duration of blockade		
Sensory, minutes	180 (80)	117* (38)
Motor, minutes	372 (140)	201** (64)

* $p < 0.01$, ** $p < 0.001$.

Surgery was totally painless for all mothers in the bupivacaine group. Only 11 patients (55%) of those given cinchocaine had comparable analgesia, and the difference was of statistical significance (Table 3). Of the remaining nine

Table 3. Efficacy of sensory block during surgery.

Category	Cinchocaine (<i>n</i> = 20)	Bupivacaine (<i>n</i> = 20)
A (painless)	11	20*
B (discomfort, no analgesia)	4	0
C (discomfort/pain, analgesia required)	3	0
D (general anaesthesia after surgery begun)	1	0
E (general anaesthesia before surgery)	1	0

* $p < 0.01$.

patients, two required general anaesthesia, one after surgery had begun and the other to allow surgery to begin, and seven experienced pain or discomfort, three of whom were given supplemental analgesia.

The incidence of complications was similar in both groups, and there were no statistical differences in any of the indices recorded (Table 4). Hypotension was a frequent

Table 4. Incidence of complications. Values expressed as number of patients (%).

	Cinchocaine (<i>n</i> = 20)	Bupivacaine (<i>n</i> = 20)	
Hypotension	10 (50%)	13 (65%)	NS
Nausea	12 (60%)	9 (45%)	NS
Vomiting	1 (5%)	0	NS
Shivering	2 (10%)	2 (10%)	NS
Urinary retention	0	0	NS
Postural headache	2 (10%)	1 (5%)	NS

NS, not significant.

complication in both groups, and occurred in 50% of mothers given cinchocaine and in 65% who received bupivacaine.

The incidence of nausea was also high, in parallel with the hypotension seen, but only one patient vomited in association with hypotension. The latter was corrected rapidly with intravenous ephedrine, and nausea usually abated when this was achieved. The mean decrease in arterial blood pressure from the pre-injection resting systolic

Table 5. Condition of neonates.

	Cinchocaine (<i>n</i> = 18)*	Bupivacaine (<i>n</i> = 20)	
Apgar score at 1 minute			
less than 7	1	0	NS
7-8	5	3	NS
9-10	12	17	NS
Apgar score at 5 minutes			
less than 7	0	0	NS
7-8	0	0	NS
9-10	18	20	NS
Time to sustained respiration (seconds)			
less than 30	16	20	NS
30-60	1	0	NS
60-120	1	0	NS

* Two mothers received general anaesthetic.

NS, not significant.

value, was 37 mmHg (SD 14) for cinchocaine and 34 mmHg (SD 17) for bupivacaine. The lowest value recorded was 55 mmHg systolic, and this occurred 20 minutes after injection of cinchocaine.

The condition of the neonates was satisfactory as assessed for both patient groups (Table 5). Apgar scores at 5 minutes were all 9 or greater, and only one neonate took longer than 60 seconds to establish sustained respiration. A retrospective diagnosis of placental insufficiency accounted for this anomaly. There was no evidence of fetal acidosis or hypoxia in the samples taken from the umbilical vein at birth.

Discussion

Our data indicate that both trial solutions produced rapid onset of sensory analgesia to mid-spinal levels of T₆ and above bilaterally. It was possible to commence surgery within 10–15 minutes of lumbar puncture in 39 of 40 cases and, in these, sensory levels persisted at or above T₆ for the duration of surgery.

The predominant difference that existed between bupivacaine and cinchocaine was in the quality and depth of analgesia. With 2.5 ml heavy bupivacaine, analgesia was complete for the whole procedure in all cases. In direct contrast, only 55% of patients who received 2.0 ml heavy cinchocaine had a comparable degree of analgesia. The pain was mainly visceral in origin in the remaining 45%, who experienced varying degrees of pain and discomfort (Table 3), often as a result of surgical manipulation of the uterus. Visceral pain has also been described when a smaller dose and volume of 0.5% heavy bupivacaine were used for Caesarean section, and when the subarachnoid injection was made with the patient sitting up.⁵ It is reassuring to note that with our method of positioning the patients for lumbar puncture in a left lateral posture and immediately returning them to a wedged, horizontal position, we have not seen blockade that extended to cervical or bulbar/cranial levels. This problem was recently described by Bembridge *et al.*⁶ when 1.5 ml lignocaine 5% was employed for Caesarean section under spinal anaesthesia.

Isobaric 0.5% bupivacaine plain has also been shown to be unpredictable in this respect in pregnant women.^{2–4,7} It is sometimes difficult in nonpregnant patients to extend blockade to upper thoracic levels.^{8–10} Our own anecdotal experience with isobaric bupivacaine has also been variable, and determined its exclusion from this study.

Hypotension and nausea occurred with equal frequency in both groups, despite preloading the circulation with 1.5 litres of Ringer's lactate and the avoidance of aortocaval compression. The incidence of 50–65% compares with other published data where preloading alone was used to prevent hypotension in patients who underwent Caesarean section with spinal anaesthesia.^{7,11} The degree of hypotension seen was at times worryingly profound, although there was no evidence of related neonatal depression, probably because the hypotension was corrected rapidly with intravenous ephedrine. Marx *et al.*¹² and Corke *et al.*¹³ showed that acidosis is present only when hypotension is prolonged, and neonatal outcome need not be adversely affected provided that hypotension is corrected rapidly. However, it is difficult to recommend subarachnoid anaesthesia as routine for Caesarean section unless

adequate precautions are taken to prevent profound hypotension, for example by prophylactic intramuscular or intravenous ephedrine infusion regimens as described by Gutsche¹⁴ and Yang *et al.*¹⁵

Postural headache was appreciable at 5–10% incidence and we were disappointed that the use of 26-gauge spinal needles throughout the study did not further reduce the incidence. The duration of analgesia with 0.5% heavy bupivacaine was significantly shorter than with 0.5% heavy cinchocaine, although the large standard deviations of the durations illustrate the variability seen with both drugs. In fact, the earliest onset of postoperative pain was only 50 minutes from spinal injection in one of the bupivacaine patients, which was only 40 minutes after the start of surgery. This must inevitably qualify any remarks about the suitability of 0.5% heavy bupivacaine for routine use as a spinal anaesthetic for Caesarean section. It would not be an appropriate agent to use if a prolonged or difficult surgical procedure is anticipated, and it is preferable that the surgeon is scrubbed and waiting whilst the spinal is performed, so that the duration of analgesia can be used to the full. Perhaps a 0.75% heavy preparation might confer a longer duration of action and maintain a predictable level of sensory analgesia. In a recent study of heavy lignocaine for elective Caesarean section,⁶ an assessment was made of the suitability of this solution for use in circumstances of failed intubation. Lignocaine was found to be unpredictable and produced dysphagia and high cervical blockade in four of 30 patients. If spinal anaesthesia is chosen as a method of managing failed intubation, then 0.5% heavy bupivacaine would appear to be a safer alternative because of the greater predictability of the height of the block.

The decision to adopt spinal anaesthesia in operative obstetrics is usually based on an ability to effect rapid onset of profound blockade and muscular relaxation when an extradural catheter is not in place. The commercial availability of local anaesthetics for intrathecal use is now severely restricted, since heavy cinchocaine ceased to be available during completion of this study. The desired production of spinal anaesthesia to T₆ for Caesarean section¹⁶ is attained more reliably with a hyperbaric agent, as opposed to an isobaric or hypobaric agent such as 0.5% plain bupivacaine, because of the unpredictable nature of the latter. Heavy bupivacaine 0.5% has been proven to be an effective spinal anaesthetic in nonpregnant patients,^{17,18} where larger volumes are necessary to produce mid-spinal anaesthesia. Our experience with heavy bupivacaine 0.5% in obstetrics, suggests that it may provide a suitable replacement for heavy cinchocaine 0.5%, with the qualifications expressed above as regards duration of action.

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References

1. THORNBURN J, MOIR DD. Epidural analgesia for elective Caesarean section. Technique and its assessment. *Anaesthesia* 1980; 35: 3–6.
2. RUSSELL IF. Intrathecal bupivacaine 0.5% for Caesarean section. *Anaesthesia* 1982; 37: 346–7.

3. RUSSELL IF. Inadvertent total spinal for Caesarean section. *Anaesthesia* 1985; **40**: 199–200.
4. STONHAM J, MOSS P. The optimal test dose for epidural anaesthesia. *Anesthesiology* 1983; **58**: 389–90.
5. SANTOS A, PEDERSEN H, FINSTER M, EDSTROM H. Hyperbaric bupivacaine for spinal anaesthesia in Cesarean section. *Anesthesia and Analgesia* 1984; **63**: 1009–13.
6. BEMBRIDGE M, MACDONALD R, LYONS G. Spinal anaesthesia with hyperbaric lignocaine for elective Caesarean section. *Anaesthesia* 1986; **41**: 906–9.
7. RUSSELL IF. Spinal anaesthesia for Caesarean section. The use of 0.5% bupivacaine. *British Journal of Anaesthesia* 1983; **55**: 309–14.
8. LOGAN MR, MCCLURE JH, WILDSMITH JAW. Plain bupivacaine: an unpredictable spinal anaesthetic agent. *British Journal of Anaesthesia* 1986; **58**: 292–6.
9. CHAMBERS WA, EDSTROM HH, SCOTT DB. Effect of baricity on spinal anaesthesia with bupivacaine. *British Journal of Anaesthesia* 1981; **53**: 279–82.
10. CAMERON AE, ARNOLD RW, GHORIS MW, JAMIESON V. Spinal analgesia using bupivacaine 0.5% plain. Variation in the extent of the block with patient age. *Anaesthesia* 1981; **36**: 318–22.
11. CLARK RB, THOMPSON DS, THOMPSON CH. Prevention of spinal hypotension associated with Cesarean section. *Anesthesiology* 1976; **45**: 670–4.
12. MARX GF, LUYKX WM, COHEN A. Fetal–neonatal status following Caesarean section for fetal distress. *British Journal of Anaesthesia* 1984; **56**: 1009–12.
13. CORKE BC, DATTA S, OSTHEIMER GW, WEISS JB, ALPER MH. Spinal anaesthesia for Caesarean section. The influence of hypotension on neonatal outcome. *Anaesthesia* 1982; **37**: 658–62.
14. GUTSCHE BB. Prophylactic ephedrine preceding analgesia for Cesarean section. *Anesthesiology* 1976; **45**: 462–5.
15. YANG YG, ABOULEISH E, CARITIS S. Prophylactic intravenous ephedrine infusion during spinal anaesthesia for cesarean section. *Anesthesia and Analgesia* 1982; **61**: 839–42.
16. LEE JA, ATKINSON RS, WATT MJ. *Sir Robert Macintosh's lumbar puncture and spinal analgesia*, 5th edn. Edinburgh: Churchill Livingstone, 1985.
17. AXELSSON KH, EDSTROM HH, SUNDBERG AEA, WIDMAN GB. Spinal anaesthesia with hyperbaric 0.5% bupivacaine; effects of volume. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 439–45.
18. SUNDNES KO, VAAGENES P, SKRETTEING P, LIND B, EDSTROM HH. Spinal analgesia with hyperbaric bupivacaine: effects of volume of solution. *British Journal of Anaesthesia* 1982; **54**: 69–73.

A single dose epidural technique for Caesarean section

A comparison between 0.5% bupivacaine plain and 0.5% bupivacaine with adrenaline

R. S. LAISHLEY AND B. M. MORGAN

Summary

An epidural technique based on a fractionated injection through a Tuohy needle of 20 ml over 10 minutes, was investigated in 40 mothers who underwent elective Caesarean section. Mothers were randomised to receive either 0.5% bupivacaine plain or 0.5% bupivacaine with adrenaline 1:200 000. After a 2-ml test dose, the remaining 18 ml was injected over 5 minutes. The use of adrenaline did not significantly alter the onset or duration, but improved the efficacy of the epidural block. Mean time to onset of adequate surgical anaesthesia was 20 minutes. Only 10 patients required more than the initial 100 mg of bupivacaine. Epidural anaesthesia was supplemented in eight patients with nitrous oxide and/or intravenous opioids.

Key words

Anaesthetic techniques, regional; epidural.

Anaesthetics, local; bupivacaine.

The incremental catheter technique¹ for elective Caesarean section has gained popularity in the United Kingdom but it suffers from the disadvantages of a prolonged induction time and the need for large doses of local anaesthetic which may result in toxicity.² Single dose catheter techniques have been used and may be more efficient.^{3,4} Injection of the full dose of local anaesthetic through the epidural needle as opposed to the catheter, may improve epidural analgesia in labour.⁵ Epidural adrenaline has been reported to reduce plasma concentrations of bupivacaine following epidural analgesia during labour.⁶

If a single slow injection of local anaesthetic leads to a reduction of total dose requirement, shortened induction to incision time and improved success rate, then epidural anaesthesia for Caesarean section might be more applicable than currently accepted. We describe the details and results of an epidural technique using a single fractionated injection administered through the needle, in which we also investigated the effect of adrenaline on epidural block.

Method

Forty healthy mothers scheduled for elective Caesarean section under epidural anaesthesia were studied following ethical committee approval and with informed consent. They were randomly allocated in a double-blind manner to receive either 0.5% bupivacaine plain or 0.5% bupivacaine

with adrenaline 1:200 000, injected through a Tuohy needle in a single 20-ml fractionated dose.

Epidural technique

Each patient was positioned on the operating table in the left lateral position with 10° foot-down tilt, following 30 ml oral 0.3M sodium citrate. An intravenous infusion of Hartmann's solution was established and continuous ECG monitoring commenced. The epidural space was located with a 16-gauge Tuohy needle at L_{2/3} or L_{3/4}. A 2-ml test dose of the selected local anaesthetic was then injected through the Tuohy needle. After 5 minutes, the remaining 18 ml was injected over 5 minutes. An epidural catheter was subsequently inserted to lie 3 cm within the epidural space. The mother was immediately turned to the other side for the next 5 minutes and thereafter placed supine, wedged, with a left lateral tilt. After rapid infusion of the first litre of Hartmann's solution, a second litre was commenced usually coincident with the epidural injection.

Assessment of epidural block

Onset of sympathetic blockade, as indicated by warm and/or vasodilated feet, was assessed at 5, 10 and 15 minutes following the end of epidural injection. Onset of motor blockade was assessed at 10, 15, 20, 25 and 30 minutes.

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Motor blockade was graded as follows: 0, no motor block; 1, impaired straight leg raising; 2, unable to achieve straight leg raising. Onset of sensory block was assessed at 15, 20, 25 and 30 minutes. Dermatome spread of sensory block was assessed using absence of perception of the cold sensation from an ethyl chloride spray. A further epidural dose (7–10 ml) of bupivacaine 0.5% was given if the spread of the block was below T_6 at 20 minutes (in one patient, 75 mg was given because of a delay in starting the operation).

The onset of adequate block for surgical anaesthesia was judged arbitrarily by the combination of bilateral sympathetic block, grade 1 or 2 motor block and sensory spread of block from S_5 to at least T_4 . Any pain or discomfort experienced during surgery was treated by one or more of the following: inhalation of 50% nitrous oxide in oxygen, a further epidural dose of bupivacaine or, after delivery of the infant, intravenous opioid analgesia.

Monitoring and progress

Pulse rate and arterial blood pressure were recorded every 5 minutes and the ECG monitored continuously. Significant hypotension was defined as a systolic arterial pressure less than 100 mmHg or a 20% decrease in systolic pressure compared to the pre-epidural measurement. This was treated promptly by increasing the intravenous infusion rate, followed by full lateral tilt and ephedrine 15 mg intravenously, with 15 mg intramuscularly if the condition remained uncorrected. Nausea was treated by correction of any associated hypotension and by intravenous metoclopramide. Oxygen, via an MC mask, was administered to all mothers from the start of surgery until delivery of the infant. Postoperatively, all mothers were visited at 24–48 hours to review their opinion of epidural anaesthesia and to assess recovery from the block. Each patient was asked to record the time of subjective return of normal motor function to her lower limbs. The time to administration of the first postoperative analgesic was recorded as an indication of recovery of sensation.

Statistics

Statistical evaluation of the data was carried out using the SAS statistical package on the Amdahl /78 computer at the University of London Computer Centre. Intergroup differences were examined by the Chi-squared test, Fisher's exact test, Student's *t*-test or the Wilcoxon rank sum test. Values of $p < 0.05$ were considered to indicate significance.

Results

The mean age, weight and height of the two groups did not differ significantly. Overall, mean age was 29.9 years (SD 6.3), weight 74.1 kg (SD 12.7) and height 1.64 m (SD 0.08). Total doses of bupivacaine for the two groups were not significantly different (Table 1). Only one patient received more than one supplementary dose. This patient was unusual in the series and received 275 mg of bupivacaine, which consisted of the initial 100 mg plus three supplementary doses given over a 2-hour period.

Onset of epidural block

The use of adrenaline did not significantly affect the onset

Table 1. Total doses of bupivacaine* (numbers of patients).

Total dose (mg)	Bupivacaine 0.5% plain (<i>n</i> = 20)	Bupivacaine 0.5% + adrenaline (<i>n</i> = 20)
100	13	17
135	2	0
140	2	0
150	2	3
275	1	0

*Total dose consists of initial 100 mg plus supplementary doses if administered.

of epidural block and therefore the data for all 40 patients were combined to document the onset of sympathetic, motor and sensory block (Fig. 1). Five patients (12.5%) required a further epidural dose to correct insufficient

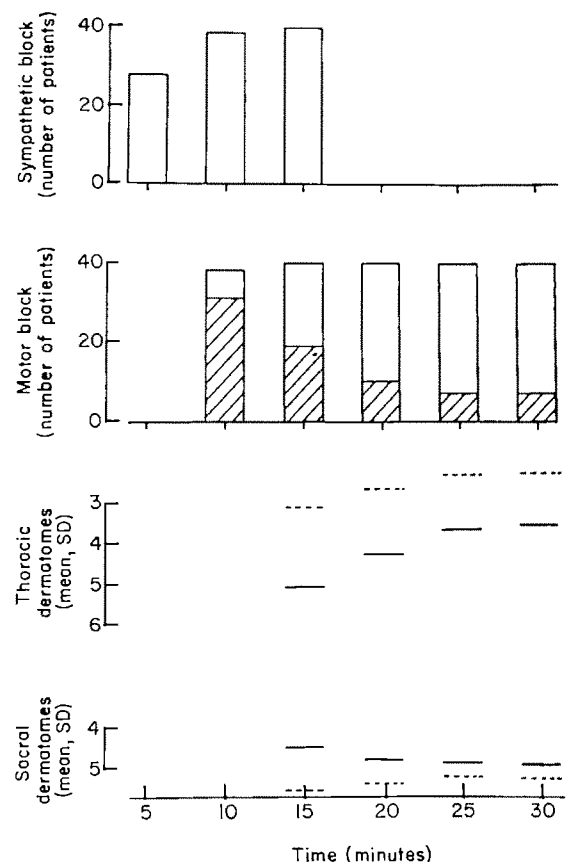


Fig. 1. Onset of sympathetic, motor and sensory (thoracic and sacral) epidural block in all patients ($n = 40$), plotted against time (minutes). Motor block: ■, grade 1; □, grade 2. Sensory block: —, mean level; ---, SD.

height of block at 20 minutes. Two patients, including one from the previous five, received a further epidural dose to maintain the block because of delayed surgical start. The mean interval from end of epidural injection to adequate surgical block was 20 minutes (SD 6.0).

Adequacy of epidural block

The requirement for analgesic supplementation after the initial 100-mg dose is summarised in Table 2. Analgesic supplementation was administered as a result of inadequate spread of block, surgical delay or intra-operative discomfort. Significantly fewer patients in the adrenaline group

Table 2. Requirements for supplementary analgesia following the initial 100-mg bupivacaine dose (numbers of patients).

Supplementary analgesia	Bupivacaine 0.5% plain (n = 20)	Bupivacaine 0.5% + adrenaline (n = 20)
Nil	11*	15*
Extra bupivacaine only	3	3
Nitrous oxide only†	2	1
Opioids only	0	1
Bupivacaine plus nitrous oxide†	1	0
Bupivacaine plus opioids	1	0
Bupivacaine, nitrous oxide† and opioids	2	0
General anaesthesia	0	0

* $p < 0.05$. Significantly fewer patients in the adrenaline group required supplementary analgesia.

† Nitrous oxide administered with 50% oxygen.

required supplementary analgesia compared to the plain group ($p < 0.05$). In no patient was general anaesthesia required for inadequate block.

Cardiovascular changes and complications

Pulse rate and arterial pressure were analysed only during the first 30 minutes after institution of the block, while the influence of surgical stimulation was absent. There was no significant difference in pulse rates or in the incidence of hypotension between patients who received bupivacaine plain and those who received bupivacaine with adrenaline. In total, transient hypotension occurred in 11 patients (27.5%); six mothers who received plain bupivacaine were given ephedrine, compared to five who received bupivacaine with adrenaline.

Nausea was highly associated ($p < 0.001$) with hypotension and often presaged it. In total, 14 patients suffered nausea during the first 30 minutes after institution of the epidural block. In addition, four patients suffered reflex nausea intra-operatively during abdominal manipulation. There was no significant difference between the groups in the incidence of nausea, which responded in all cases to correction of hypotension, administration of metoclopramide and removal of surgical stimulus. Shivering occurred in 13 patients in the adrenaline group and six patients in the plain group. This difference was statistically significant ($p < 0.05$).

Condition of the infant

There were no significant differences in the Apgar scores achieved by infants from the two groups. Overall, 22 infants (55%) had a one-minute Apgar score of 9 or 10, and 17 infants (42.5%) had a score between 5 and 8. All infants had a 5-minute Apgar score of 10.

Postoperative recovery

Thirty-five mothers (87.5%) were pleased and satisfied, while four found the experience disturbing. Intra-operative analgesia was required by 10 mothers but only one reported intra-operative pain retrospectively.

There was no significant difference in sensory and motor recovery intervals between the two groups. The mean sensory recovery time was 286 minutes (SD 84) for the bupivacaine plain group and 311 minutes (SD 72) for the

bupivacaine with adrenaline group. The mean times for recovery of motor function were 303 minutes (SD 100) and 330 minutes (SD 109), respectively, for the two groups.

Discussion

We have investigated an epidural technique based on fractionated injection through a Tuohy needle and demonstrated that it is safe, efficient and effective. Compared to other series^{1,2} our mothers received lower doses of local anaesthetic, which offer advantages to both mother and fetus.⁷ A standardised epidural technique and method of assessment of block were used in order to improve efficiency and facilitate the teaching of epidural anaesthesia to junior anaesthetists.

Epidural injection through the Tuohy needle is widely practised but there are few reports of its use in obstetrics. Mehta *et al.*⁵ reported improved analgesia during labour following epidural injection through the needle, although the mechanism for this is not clear. We fully advocate the use of a test dose, with continuous ECG monitoring and observation of the patient. There is no advantage from rapid epidural injection⁸ and the dose was therefore given by slow fractionated injection, which may improve safety when large doses of local anaesthetic are used. Injection through the Tuohy needle avoids the hazard of accidental dural or vascular puncture by the catheter. Subsequent insertion of the epidural catheter allows flexibility of technique. Various methods to assess the onset of epidural blockade have been described^{9,10} but our sequence was designed to provide the maximum useful information with minimal patient anxiety. Bilateral warm, dry feet are the earliest confirmatory sign of the onset of sympathetic block and can be assessed without patient disturbance.

We interpreted the degree of motor blockade of the hip flexors as an indication of the density of epidural block. This is confined to the L_{1/2} myotomes and does not represent abdominal musculature but it does indicate the density of block in the mid-range of the spinal segments affected. The three grades of motor blockade, as tested by straight leg raising, have simply defined endpoints (i.e. absent or complete motor weakness), and can be assessed quickly with minimal patient disturbance. The Bromage technique,⁹ which includes evaluation of more distal motor blockade, may not be relevant to abdominal surgery. The RAM test¹⁰ is more complex, with six degrees of motor blockade. Dissociation of pain and temperature is unusual in epidural analgesia.¹¹ The perception of cold sensation rather than pinprick, may minimise patient anxiety when sensory spread of block is assessed. Assessment of sensory spread is probably not necessary before 15 minutes, provided that there are no adverse changes in the patient's vital functions. We consider that proper systematic assessment of epidural blockade may improve the results of epidural anaesthesia and aid in the teaching of this technique to junior anaesthetists.

The use of adrenaline in solutions of local anaesthetics for epidural analgesia in obstetrics has previously been controversial. Recent studies by Abboud *et al.*^{12,13} indicated that epidural adrenaline is not deleterious and has no significant effect on uterine activity, duration of labour or fetal heart rate when used with lignocaine or bupivacaine solutions. The intensity and duration of epidural blockade with lignocaine may be increased by adrenaline,¹⁴ but this

effect has been described to be not so significant with bupivacaine.¹⁵ Reynolds and Taylor¹⁶ found that the duration of action of 0.5% bupivacaine was not prolonged by adrenaline in epidural analgesia for labour. Our results indicate that adrenaline 1:200 000 does not affect significantly the speed of onset or duration of block, but does improve the effectiveness of surgical anaesthesia for elective Caesarean section.

In this study epidural adrenaline did not have a significant effect on pulse rate or arterial blood pressure. In contrast, Bonica *et al.*,¹⁷ who used lignocaine 2% in normal non-pregnant volunteers, found that epidural adrenaline in the same dose was associated with a significant decrease in mean arterial pressure and total peripheral resistance. They suggested that this was probably produced by predominantly beta-adrenergic vasodilatation and that a synergistic action existed between adrenaline and the vasomotor blockade produced by epidural local anaesthesia. The lack of this observed effect in our study may be explained by the use of fluid loading and a local anaesthetic with greater latency of action.

Hypotension occurred in 27.5% of patients in our study, compared to 16% in Thorburn and Moir's series¹ and 14.4% in Crawford's,² both of which used the incremental technique. Crawford¹⁸ has suggested that maternal hypotension is more unusual if the incremental technique is used, but a lower incidence of hypotension is gained at the expense of prolonging the time to establish the block and by the use of larger doses of bupivacaine. An unusually low incidence of hypotension (6.6%) was reported by Lewis *et al.*¹⁹ who used an epidural technique and preload similar to our method. They described the use of manual uterine displacement rather than buttock wedging, which may imply that the former is more effective in the prevention of hypotension. The effect of different volumes and solutions of preload on placental perfusion and the fetus itself has not been elucidated and caution seems to be justified, with the use of modest volumes of crystalloid. We fully advocate the use of ephedrine, which has been reported to preserve placental intervillous blood flow²⁰ whilst it corrects hypotension probably by constriction of the venous capacitance vessels.²¹

Thompson *et al.*²² reported high plasma bupivacaine concentrations (mean maximum 1506 ng/ml) following a single bolus dose of 20 ml 0.5% bupivacaine given over 20 seconds. The results of plasma bupivacaine analysis in our series of slow fractionated injections do not support their findings. These results and a full discussion are reported separately.²³

In conclusion, epidural adrenaline may improve the effectiveness of 0.5% bupivacaine for surgical anaesthesia. We suggest that this technique represents an improvement over the results described in other series,^{1,2} in that 65% of our mothers received only 100 mg bupivacaine for Caesarean section. In addition, a reduction of anaesthetic time reduces the duration of maternal stress and makes epidural block for Caesarean section a practical technique in most hospitals.

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References

1. THORBURN J, MOIR DD. Epidural analgesia for elective

- Caesarean section. Technique and its assessment. *Anaesthesia* 1980; **35**: 3-6.
2. CRAWFORD JS, DAVIES P, LEWIS M. Some aspects of epidural block provided for elective Caesarean section. *Anaesthesia* 1986; **41**: 1039-46.
3. ABBOUD TK, KIM KC, NOUEITHED R, KUHNERT BR, DERMARDIROSIAN N, MOUMDIAN J, SARKIS F, NAGAPPALA S. Epidural bupivacaine, chloroprocaine or lidocaine for Caesarean section—maternal and neonatal effects. *Anesthesia and Analgesia* 1983; **62**: 914-9.
4. DATTA S, ALPER MH, OSTHEIMER GW, BROWN WU, WEISS JB. Effects of maternal position on epidural anaesthesia for Caesarean section, acid base status, and bupivacaine concentrations at delivery. *Anesthesiology* 1979; **50**: 205-9.
5. MEHTA P, THERIOT E, MEHROTRA D, PATEL K, MEHTA D, TAHVILDARI F, ZARBALIAN A. Technique of injection, maternal position and spread of anesthetic in epidural anaesthesia. *Anesthesiology* 1983; **59**: A410.
6. REYNOLDS F, HARGROVE RL, WYMAN JB. Maternal and foetal plasma concentrations of bupivacaine after epidural block. *British Journal of Anaesthesia* 1973; **45**: 1049-53.
7. RALSTON DH, SHNIDER SM. The fetal and neonatal effects of regional anaesthesia in obstetrics. *Anesthesiology* 1978; **48**: 34-64.
8. HUSEMEYER RP, WHITE DC. Lumbar extradural injection pressures in pregnant women. An investigation of relationships between rate of injection, injection pressures and extent of analgesia. *British Journal of Anaesthesia* 1980; **52**: 55-60.
9. BROMAGE PR. A comparison of the hydrochloride and carbon dioxide salts of lignocaine and prilocaine in epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1965; **16** (Suppl.): 55-69.
10. VAN ZUNDELT A, VAES L, VAN DER AA P, VAN DER DONCK A, MEEUWIS H. Motor blockade during epidural anaesthesia. *Anesthesia and Analgesia* 1986; **65**: 333-6.
11. BROMAGE PR. Physiology and pharmacology of epidural analgesia. *Anesthesiology* 1967; **28**: 592-622.
12. ABBOUD TK, DAVID S, NAGAPPALA S, COSTANDI J, YANAGI T, HAROUTUNIAN S, YEH SU. Maternal, fetal and neonatal effects of lidocaine with and without epinephrine for epidural anaesthesia in obstetrics. *Anesthesia and Analgesia* 1984; **63**: 973-9.
13. ABBOUD TK, SHEIK-OL-ESLAM A, YANAGI T, MURAKAWA K, COSTANDI J, ZAKARIAN M, HOFFMAN D, HAROUTUNIAN S. Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. *Anesthesia and Analgesia* 1985; **64**: 585-91.
14. BROMAGE PR. A comparison of the hydrochloride salts of lignocaine and prilocaine for epidural analgesia. *British Journal of Anaesthesia* 1965; **37**: 753-61.
15. COVINO BG. Pharmacology of local anaesthetic agents. *British Journal of Anaesthesia* 1986; **58**: 701-16.
16. REYNOLDS F, TAYLOR G. Plasma concentration of bupivacaine during continuous epidural analgesia in labour: the effect of adrenaline. *British Journal of Anaesthesia* 1971; **43**: 436-9.
17. BONICA JJ, AKAMATSU TJ, BERGES PU, MORIKAWA K, KENNEDY WF. Circulatory effects of peridural block. II. Effects of epinephrine. *Anesthesiology* 1971; **34**: 514-22.
18. CRAWFORD JS. Experiences with lumbar extradural analgesia for Caesarean section. *British Journal of Anaesthesia* 1980; **52**: 821-4.
19. LEWIS M, THOMAS P, WILKES RG. Hypotension during epidural analgesia for Caesarean section. Arterial and central venous pressure changes after acute intravenous loading with two litres of Hartmann's solution. *Anaesthesia* 1983; **38**: 250-3.
20. HOLLMER AI, JOUPPIA R, ALBRIGHT GA, JOUPPIA P, VIEROLA H, KOIVULA A. Intervillous blood flow during Caesarean section with prophylactic ephedrine and epidural anaesthesia. *Acta Anaesthesiologica Scandinavica* 1984; **28**: 396-400.
21. RAMANATHAN S, GRANT G, TURNDOFF H. Cardiac preload changes with ephedrine therapy for hypotension in obstetrical patients. *Anesthesia and Analgesia* 1986; **65**: S125.
22. THOMPSON EM, WILSON CM, MOORE J, MCCLEAN E. Plasma bupivacaine levels associated with extradural anaesthesia for Caesarean section. *Anaesthesia* 1985; **40**: 427-32.
23. LAISHLEY RS, MORGAN BM, REYNOLDS F. Effect of adrenaline on extradural anaesthesia and plasma bupivacaine concentrations during Caesarean section. *British Journal of Anaesthesia* 1988; **60**: 180-6.



Peri-operative dreaming in paediatric patients who receive suxamethonium

E. P. O'SULLIVAN, D. CHILDS AND G. H. BUSH

Summary

A prospective study is described of peri-operative dreaming in 144 paediatric patients aged 5–14 years who received suxamethonium for day case surgery. No case of awareness was elicited. One group received pretreatment with 80 mg/kg tubocurarine. The incidence of dreaming in the 72 patients who were not pretreated was 16.7% compared with 2.8% in the patients pretreated with tubocurarine. This difference is statistically significant. The use of an intermittent suxamethonium technique gives a high incidence of dreaming which may be caused by muscle spindle discharge that produces cerebral arousal. Pretreatment with a non-depolarising agent decreases this risk of dreaming.

Key words

Complications; dreaming.

Neuromuscular relaxants; suxamethonium.

There have been many studies of dreaming and awareness during anaesthesia in adults, but few in children. Hobbs *et al.*¹ performed a prospective study of 373 children aged 5–16 years who were anaesthetised using the 'Liverpool technique' of paediatric anaesthesia (nitrous oxide/oxygen/muscle relaxant). A much higher incidence of dreaming was observed in day case patients who had received suxamethonium than in any other single group. A large synchronous afferent stimulus from muscle spindle discharge after suxamethonium administration has been implicated in the production of an arousal-type electroencephalograph (EEG) pattern in adults and children; this pattern can be abolished by pretreatment with a non-depolarising muscle relaxant.² The purpose of the present study was to determine whether pretreatment with a non-depolarising relaxant would result in a reduction in the incidence of dreaming in children who received suxamethonium.

Method

A prospective study was carried out on 144 patients (84 male) aged 5–14 years, who underwent day case surgery for which suxamethonium was indicated clinically. The

patients received either no premedication, 'Ponstan Mix' (a mixture of trimeprazine, mefenamic acid and atropine) or pethidine and atropine. They were allocated into one of two groups depending on their date of birth. Patients with an even birth date received pretreatment with 80 µg/kg tubocurarine one minute before induction of anaesthesia; those with an odd birth date received no pretreatment. A standard anaesthetic was used, which consisted of an induction dose of thiopentone 5 mg/kg, atropine 20 µg/kg, suxamethonium 1.5 mg/kg and tracheal intubation. The patients' lungs were ventilated manually using an Ayre's T-piece with the Jackson-Rees modification with a mixture of 70% nitrous oxide and 30% oxygen; increments of suxamethonium were given as required during the procedure. Details of the patient, anaesthetic, operation, presence or absence of fasciculations at induction and degree of intra-operative movement (none, slight, moderate) were recorded by the anaesthetist.

One observer (who was unaware of the pretreatment details) interviewed the child on return to the ward, before discharge. A standard questionnaire (Table 1) modified from Brice *et al.*³ and McKie and Thorp⁴ was used; the questions were incorporated into a conversation with the child.

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Table 1. Postoperative questionnaire.

Were you upset or worried about your operation?
What is the last thing you remember before going to sleep?
How did the doctor put you to sleep?
What is the next thing you remember after going to sleep?
Did you have any dreams or odd feelings while you were asleep?
Were you sore after the operation?
What did you like least about having an operation?
Do you have dreams at home?

Table 2. Types of surgery performed.

Surgery	n
ENT	115
Ophthalmic	3
Dental	7
Urogenital	16
Orthopaedic	3
Total	144

Results

There were 72 patients in each group. The distribution of types of surgical procedure is shown in Table 2. Two patients in the pretreatment group (2.8%) and 12 in the non-pretreated group (16.7%) had intra-operative dreams (Table 3). This difference is statistically significant ($p < 0.01$) using Fisher's test of exact probability. The mean incidence of dreaming was 9.7%. The mean age of children who dreamt was 8.7 years (range 5–16), and 8.5 years (range 5–16) in those who had no dreams. No patient had spontaneous recall of intra-operative events. There was no correlation between the incidence of peri-operative movement and dreaming (Table 4). Premedication had no significant effect on the incidence of dreaming (Table 5).

Table 3. Incidence of peri-operative dreaming.

	Number reporting dreams	(%)
Pretreated patients ($n = 72$)	2	(2.8%)*
Untreated patients ($n = 72$)	12	(16.7%)*

* $p < 0.05$ (χ^2 with Yates' correction), $p < 0.01$ (Fisher's test of exact probability). Overall incidence of dreaming, 14/144 (9.7%).

Table 4. Peri-operative movement and dreaming. Values represent percentage of total patients in each group, with numbers of patients in parentheses.

Peri-operative movement	Patients reporting dreams	Patients not reporting dreams	Total patients
None	9.8% (6)	90.2% (55)	61
Slight	9.8% (7)	90.2% (64)	71
Moderate	8.3% (1)	91.7% (11)	12
Total numbers of patients	14	130	144

Not significant.

Table 6. Incidence of dreaming at home.

	Number of home dreamers (%)
Patients reporting peri-operative dreams ($n = 14$)	8 (57%)
Patients not reporting peri-operative dreams ($n = 130$)	84 (65%)

There was no significant difference between the numbers of patients in the dreaming and non-dreaming groups who reported dreams at home (Table 6).

Discussion

The mean incidence of dreaming in this study (9.7%) corresponds well with the work which Pledger⁵ performed 25 years ago. He found that 11% of 431 children anaesthetised with the 'Liverpool technique' (nitrous oxide/oxygen/muscle relaxant) had dreamed. Hobbs *et al.*,¹ who used the same technique, found that 12% of 373 children had dreamed. The relaxant used in both studies was either curare or suxamethonium. All children in the present study received suxamethonium. The incidence of dreaming in the patients who were not pretreated was 16.7% compared with 2.8% in the patients pretreated with tubocurarine and this difference is statistically significant.

A number of mechanisms must be considered to explain these results. Riker and Okamoto⁶ demonstrated that suxamethonium can induce both prodromic and antidromic firing of nerve tissue. Thus it is theoretically possible that impulses generated by suxamethonium may enter the central nervous system in both an anterograde and retrograde fashion. However, according to existing theories of neurotransmission, only prodromic impulses should be transmitted to the brain. Antidromic impulses would not be able to pass retrogradely through the first synapse encountered, and the wave of depolarisation would cease. It is unlikely that suxamethonium can cross the blood-brain barrier in an amount sufficient to produce cerebral arousal. Motokizawa and Fujimori⁷ found that intravenous suxamethonium produced EEG arousal in cats but suxamethonium injected into the carotid arteries had no effect on the EEG.

The absence of cerebral stimulation in dogs pretreated with a non-depolarising muscle relaxant supports the theory that cerebral stimulation by suxamethonium is dependent on muscle activity.⁸ The administration of suxamethonium is known to increase the discharge from muscle spindles by causing intrafusal fibre contraction, which results in increased activity in muscle afferents.⁹ It has been demonstrated that this effect is preventable by pretreatment with a non-depolarising neuromuscular

Table 5. Premedication and dreaming.

	Patients reporting dreams				Patients not reporting dreams				Total
	Nil	'Ponstan Mix'	Pethidine/atropine	Subtotal (%)	Nil	'Ponstan Mix'	Pethidine/atropine	Subtotal (%)	
Pretreated group	0	2	0	2 (2.8%)	28	37	5	70 (97.2%)	72
Untreated group	5	7	0	12 (16.7%)	25	30	5	60 (83.3%)	72
Total numbers of patients				14 (9.7%)				130 (90.3%)	144

Not significant.

blocking agent.¹⁰ Recent work in a canine model found that intravenous suxamethonium induced EEG arousal.⁸ in the present study from 16.7 to 2.8%; this difference in causes an EEG pattern consistent with cortical arousal during halothane anaesthesia in humans. They found that this effect can be blocked by pretreatment with a non-depolarising neuromuscular blocker, and postulated that intrafusal fibre contraction causes this EEG arousal. Pretreatment with a non-depolarising neuromuscular blocker has been shown therefore to block the intrafusal fibre contraction and thus the EEG arousal pattern.

Pretreatment reduced the incidence of reported dreams in the present study from 16.7 to 2.8%; this difference in incidence of dreams may be related to the EEG arousal pattern associated with suxamethonium. However, further investigation is required to explain fully the mechanisms involved. For example, the precise timing of the dreams is not known in relation to intra-operative and postoperative events. It is our intention to study EEG activity during induction to determine whether there is a correlation between EEG activity following suxamethonium and subsequent report of dreaming. In addition, such a study may answer some other questions which have arisen from this investigation, for example the effect of a sleep dose of thiopentone or alternative induction agents followed by suxamethonium on EEG activity.

In conclusion, the use of an intermittent suxamethonium technique results in a high incidence of dreaming. This may be caused by intrafusal fibre contraction, increased activity in muscle afferents, and profound cerebral arousal. However, this link must remain speculative until a direct relationship between dreaming, muscle spindle activity and EEG changes has been demonstrated. Pretreatment with a non-depolarising neuromuscular blocker decreases the risk of

dreaming. It is our opinion, based on the results of this study, that a small dose of a non-depolarising agent should be administered to all children who receive suxamethonium if the increased risk of dreaming is thought to be detrimental.

References

1. HOBBS AJ, BUSH GH, DOWNHAM DY. Peri-operative dreaming and awareness in children. *Anaesthesia* (in press).
2. MORI K, IWABUCHI K, FUJITA M. The effects of depolarizing muscle relaxants on the electroencephalogram and the circulation during halothane anaesthesia in man. *British Journal of Anaesthesia* 1973; **45**: 604-10.
3. BRICE DD, HETHERINGTON RR, UTTING JE. A simple study of awareness and dreaming during anaesthesia. *British Journal of Anaesthesia* 1970; **42**: 535-41.
4. MCKIE BD, THORP EA. Awareness and dreaming during anaesthesia in a paediatric hospital. *Anaesthesia and Intensive Care* 1973; **1**: 407-14.
5. PLEDGER HG. Observations on some aspects of general anaesthesia in children. MD Thesis, Durham, 1963: 97-104.
6. RIKER WF, OKAMOTO M. Pharmacology of motor nerve terminals. *Annual Review of Pharmacology* 1969; **9**: 173-208.
7. MOTOKIZAWA F, FUJIMORI S. Arousal effect of afferent discharges from muscle spindles upon electroencephalograms in cats. *Japanese Journal of Physiology* 1964; **14**: 344-53.
8. LANIER WL, MILDE JH, MICHENFELDER JD. Cerebral stimulation following succinylcholine in dogs. *Anesthesiology* 1986; **64**: 551-9.
9. SMITH CM, ELDRED E. Mode of action of succinylcholine on sensory endings of mammalian muscle spindles. *Journal of Pharmacology and Experimental Therapeutics* 1961; **131**: 237-42.
10. GRANIT R, SKOGLUND S, THESLEFF S. Activation of muscle spindles by succinylcholine and decamethonium. The effects of curare. *Acta Physiologica Scandinavica* 1953; **28**: 134-51.
11. OSHIMA E, SHINGU K, MORI K. E.E.G. activity during halothane anaesthesia in man. *British Journal of Anaesthesia* 1981; **53**: 65-73.

Paediatric postoperative analgesia

A comparison between caudal block and wound infiltration of local anaesthetic

D. FELL, M. C. DERRINGTON, E. TAYLOR AND J. G. WANDLESS

Summary

Fifty children who underwent day case herniotomy received either a caudal injection of 1 ml/kg bupivacaine 0.25% or infiltration of the wound edges at the end of surgery with 0.5 ml/kg bupivacaine 0.25%, allocated at random. Postoperative pain and demeanour were assessed initially by an observer and later by use of a parental questionnaire. Wound infiltration of local anaesthetic solution provided analgesia which was comparable to that associated with caudal block, and the incidence of side effects was similar in the two groups. Wound infiltration of local anaesthetic offers a simple, safe alternative to caudal block for provision of postoperative analgesia in this group of patients.

Key words

Anaesthesia; paediatric.

Anaesthetic techniques, regional; caudal block, local infiltration.

Day case surgery for repair of inguinal hernia in infants and children has become accepted practice. It is particularly important in this patient group to ensure that postoperative discomfort is relieved in order to minimise for both patient and parent the stress and upset that arise from pain, and the adverse effects of analgesic drugs.¹ Techniques to provide residual postoperative analgesia include the use of parenteral opioid drugs,² caudal epidural analgesia³ and ilio-inguinal nerve block.^{4,5} Smith and Jones⁵ asserted that herniotomy is not sufficiently painful to justify the routine use of postoperative narcotic analgesics in day patients.

Local anaesthesia by wound infiltration at the end of surgery provided effective analgesia after excision of benign breast lumps⁶ and reduced the requirement for postoperative analgesia after cholecystectomy.⁷ Similarly, administration of local anaesthetic solution via a subcutaneous catheter was employed to provide effective postoperative analgesia after herniorrhaphy in adults.⁸

The purpose of this study was to compare wound infiltration of local anaesthetic solution with an established technique, namely caudal local anaesthesia, in terms of postoperative analgesia in children who underwent day case surgery for inguinal herniotomy.

Patients and methods

Fifty children who were scheduled to undergo unilateral inguinal herniotomy as day cases were admitted to the study. The children were otherwise fit and healthy and had no

intercurrent disease or concurrent medication. The nature of the investigation was explained to the accompanying parent and written consent for inclusion of the child in the trial was obtained. Date of birth and weight of each child were recorded.

No premedication was given and all operations were carried out under general anaesthesia. Anaesthesia was induced in the anaesthetic room either with thiopentone 5–6 mg/kg via a 23-gauge butterfly cannula inserted into a vein on the dorsum of the hand, or with inhalation of nitrous oxide, oxygen and halothane. Anaesthesia was maintained using nitrous oxide 67%, oxygen 33% and halothane delivered via a Bain coaxial system or Ayre's T-piece with spontaneous ventilation.

After induction of general anaesthesia, patients were assigned randomly to receive either a caudal injection of 1 ml/kg (maximum 20 ml) plain bupivacaine 0.25% (group A), or 0.5 ml/kg of the same solution injected into the edges of the wound before closure (group B). The caudal was performed in each case by one of the authors (J.G.W.) with the patient in the left lateral position, using a 23-gauge needle. Group B received an injection of local anaesthetic solution administered by the surgeon under the supervision of the anaesthetist. A small Elastoplast dressing was placed over the site of the sacral hiatus in all patients.

The concentration of volatile agent was reduced towards the end of surgery in order to achieve rapid awakening before return to the day ward. Postoperative analgesia (papaveretum 0.2 mg/kg) was prescribed for each patient

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and was given as required at the discretion of the nursing staff, who were unaware of the group allocation of the patient. Alternatively, aspirin 150–450 mg was available to be given if necessary. This was later changed to paracetamol 120–500 mg following the recommendations of the *Committee on safety of medicines* on the use of aspirin in children.

The children were assessed after return to the ward, by an independent observer (M.C.D.) who had no knowledge of the group allocation of each patient. Assessments took place at 1, 2 and 4 hours after the patients awoke. The observer scored pain on each occasion with reference to a three-point scale (none/insignificant pain, moderate pain, severe pain) and demeanour was scored similarly (cheerful and calm, restless, tense or tearful). Side effects were recorded by the observer as well as the administration, if any, of additional analgesia.

Further assessments after discharge from hospital were made by the parents, who completed a questionnaire and returned it in a stamped addressed envelope. The questionnaire asked the parent to assess the child's behaviour at bedtime on the day of operation and on the following morning in respect of pain, vomiting, oral intake, analgesic requirement, mobility (in the evening), micturition and quality of sleep (overnight). The questionnaire was similar to that employed previously.^{9,10} The data were analysed using Student's unpaired *t*-test and the Chi-squared test.

Results

The records for one patient were incomplete and therefore data that relate to the immediate postoperative period were available for analysis for 49 subjects. Twenty-two patients received caudal bupivacaine and 27 patients received wound infiltration with bupivacaine; the groups were comparable in respect of age and weight (Table 1). Three parental questionnaires were not returned, relating to two patients in group A and one patient in group B, and a further

Table 1. Mean (SD) age and weight of patients.

	Group A (caudal) (n = 22)	Group B (infiltration) (n = 27)
Age, years	4.5 (2.9)	3.7 (2.5)
Weight, kg	16.1 (6.5)	16.2 (5.5)

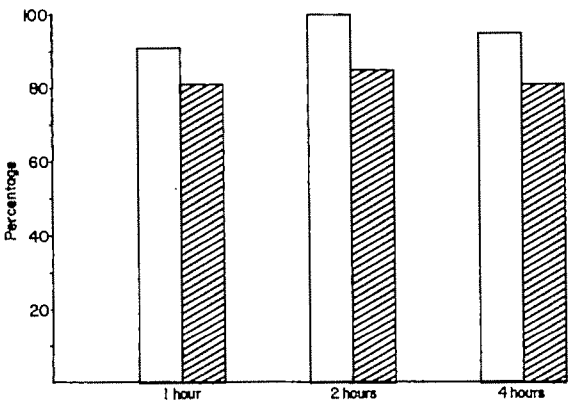


Fig. 1. Percentage of patients with satisfactory analgesia in the early postoperative phase. □, Group A (n = 22); ▨, group B (n = 27).

questionnaire from a patient in group B was incomplete. Thus, data for the later postoperative period were available for 20 patients in group A and 25 patients in group B.

Analgesia in the early postoperative period was deemed satisfactory when pain was reported as none or insignificant. Similar rates of satisfactory analgesia were achieved in each group at 1, 2 and 4 hours postoperatively (Fig. 1). Satisfactory analgesia at the evening or overnight assessments by the parent was considered to be present when no report of pain was received. Forty-two percent of those in group B and 20% of those in group A were rated to have satisfactory analgesia on the evening of the day of operation, while the figures for the overnight assessment were 64% for group B and 45% for group A (Fig. 2). The differences were

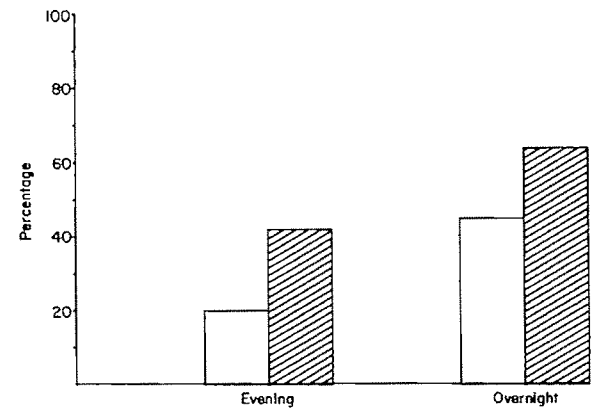


Fig. 2. Percentage of patients with satisfactory analgesia in the late postoperative phase. □, Group A (n = 20); ▨, group B (n = 25).

not significant (Chi-squared test with Yates' correction). Similarly, there were no differences between the groups in respect of analgesic requirements at any time. The maximum requirement was in the evening, when 55% of children in group A and 46% in group B required aspirin or paracetamol (Fig. 3). No patient required papaveretum during the postoperative period on the day ward.

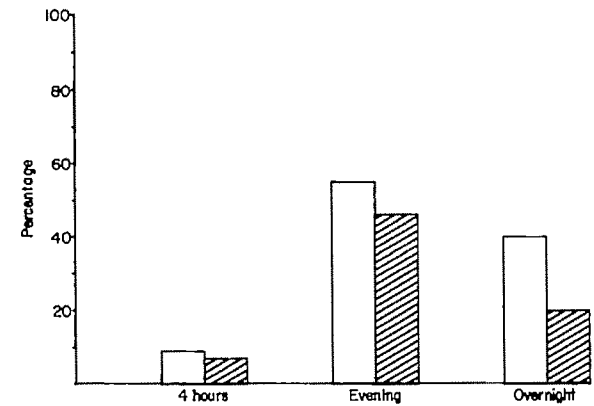


Fig. 3. Additional analgesia received by children postoperatively. Data expressed as percentage of patients. □, Group A (n = 22, 4 hours; n = 20, evening and overnight); ▨, group B (n = 27, 4 hours; n = 25, evening and overnight).

There were no differences between the groups in respect of postoperative behaviour in the early phase; the majority of patients in each group were described as cheerful and calm at 1, 2 and 4 hours postoperatively (Table 2). Nausea or vomiting occurred postoperatively at 1 hour (group A,

Table 2. Postoperative behaviour; results expressed in numbers of patients.

	Group	1 hour	2 hours	4 hours
Calm and cheerful	A	18	22	22
	B	21	25	24
Restless or tearful	A	4	0	0
	B	6	2	3

three patients; group B, four patients), 2 hours (group A, three patients; group B, four patients) and 4 hours (group A, three patients; group B, five patients). One patient (in group B) complained of headache 1 hour postoperatively. Three patients (14%) in group A had persistent numbness in the legs up to 4 hours postoperatively. Four patients were admitted to hospital overnight; three in group A (two because of persistent numbness and circulatory effects on standing, and one for surgical reasons) and one in group B (for surgical reasons).

Further results from the parental questionnaire are given in Table 3. There were no significant differences between the groups in respect of these side effects.

Table 3. Results of parental questionnaire. Data expressed as number of patients.

	Group A	Group B
Vomiting (evening)	4	7
Refused oral intake	2	0
Disturbance to normal activity	2	4
Urinary retention	2	0
Overnight vomiting	1	1
Interrupted sleep	6	4

Discussion

The results of this study demonstrate that wound infiltration with local anaesthetic solution provides a degree of postoperative analgesia comparable to that associated with the use of caudal anaesthesia in children who undergo day case herniotomy.

Mather and Mackie¹¹ reiterated the importance of the provision of adequate postoperative analgesia for children and concluded, after a survey of prescribing and administration habits, that there is much room for improvement in techniques. Kay¹² was one of the early advocates of caudal bupivacaine to provide intra- and postoperative analgesia for circumcision in day cases, and Lunn¹³ demonstrated the superiority of caudals over intramuscular morphine for postoperative analgesia.

Caudal block to provide intra- and postoperative analgesia for herniotomy in children has been practised for some time. Armitage³ advocated a dosage of 1 ml/kg bupivacaine 0.25% for herniotomy and, although other regimens exist,^{14,15} Armitage's has the advantage of simplicity, is widely employed and relates volume to weight (the usual means of calculating maximum dose). The safety of the regimen was confirmed by measurement of the maximum plasma concentrations of bupivacaine after caudal injection.¹⁶ Nevertheless, caudal injection is an invasive procedure, demands some expertise to achieve success and consumes time when performed in children after induction of anaesthesia. No advantage of the caudal technique could be demonstrated when compared with systemic analgesia provided by intramuscular injections of dihydrocodeine.²

In contrast, wound infiltration of local anaesthetic

solution is a simple procedure and can be carried out easily and quickly by the surgeon at the end of the operation. The technique is not new; infiltration via needles placed in the wound was reported in 1935.^{17,18} Its effectiveness was demonstrated in small wounds after breast biopsy in adults⁶ and after herniorrhaphy in adults.⁸ The technique is also advocated for use following cholecystectomy.⁷ No adverse sequelae attributable to infiltration of solution into the wound at closure have been reported in respect of wound healing either from our patients or from elsewhere.

The assessment and quantification of postoperative pain can be difficult in adult patients¹⁹ but it is even more difficult in children. Manifestations of pain in infants and children are multivariate and include behavioural, cognitive-experiential and biological aspects.²⁰ No attempt was made in this study to employ the last variable since this would require invasive measurement; cognitive-experiential manifestations necessitate self-reporting and are less reliable in children. We therefore placed reliance upon behavioural manifestations assessed by a trained observer who was an anaesthetist familiar with paediatric practice. The criteria were deliberately kept simple in order to contribute to the validity of judgments which could be influenced by other factors, for example, the presence of a parent. In addition, the postoperative observations were repeated at comparatively short intervals so the assessor gained a subjective comparison of the patient's behaviour which may improve the reproducibility of the measurements.

Our results reveal that between 60 and 80% of children had less than ideal analgesia when assessed by the parent on the evening of the operation. This is a slight improvement upon the experience described by Mather and Mackie,¹¹ where only 25% of patients had ideal analgesia on the operation day, but these figures emphasise the need to provide analgesia which persists into the late postoperative period. Shandling and Steward¹ suggest that postoperative analgesia is essential in the majority of children over 6 months of age. About 50% of the patients in the present study required some form of additional analgesia following discharge, although the differences between groups in respect of analgesic requirement on the evening of surgery did not achieve statistical significance. However, Bramwell *et al.*² noted a significantly greater consumption of analgesic drugs between 2 and 8 hours postoperatively in patients who received caudal analgesia in comparison to those given intramuscular dihydrocodeine. This may indicate a need for analgesia in the later postoperative period, when the effects of the block would be expected to have ceased.

The complaint of numbness in the legs in three patients in the caudal group (14%) was distressing for those children and was associated with walking difficulty in one of them. Persistent numbness is an occasional complication of caudal analgesia with bupivacaine. Yeoman *et al.*²¹ noted inability to walk in 31% of patients after caudal bupivacaine 0.5% but Vater and Wandless,¹⁰ who used a lower dose (0.5 ml/kg bupivacaine 0.25%) than in the present study, found that only 8% of patients were unable to stand at 6 hours postoperatively. Postoperative urinary retention was noted by the latter authors, who studied patients who underwent circumcision. They found a significantly greater incidence of urinary retention at 4 hours in the caudal group¹⁰ but Yeoman *et al.*,²¹ who demonstrated a 42% incidence of urinary retention at 6 hours in patients who received caudal

injections, found no difference between these patients and a group who received dorsal nerve block for analgesia. No patient in the caudal group in the present study experienced delayed discharge from hospital as a result of this complication.

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References

- SHANDLING B, STEWARD DJ. Regional analgesia for postoperative pain in pediatric outpatient surgery. *Journal of Pediatric Surgery* 1980; **15**: 477-80.
- BRAMWELL RGB, BULLEN C, RADFORD P. Caudal block for postoperative analgesia in children. *Anaesthesia* 1982; **37**: 1024-8.
- ARMITAGE EN. Caudal block in children. *Anaesthesia* 1979; **34**: 396.
- MARKHAM SJ, TOMLINSON J, HAIN WR. Ilioinguinal nerve block in children. A comparison with caudal block for intra- and postoperative analgesia. *Anaesthesia* 1986; **41**: 1098-1103.
- SMITH BAC, JONES SEF. Analgesia after herniotomy in a paediatric day unit. *British Medical Journal* 1982; **285**: 1466.
- OWEN H, GALLOWAY DJ, MITCHELL KG. Analgesia by wound infiltration after surgical excision of benign breast lumps. *Annals of the Royal College of Surgeons of England* 1985; **67**: 114-5.
- PATEL JM, LANZAFAME RJ, WILLIAMS JS, MULLEN BV, HINSHAW JR. The effect of incisional infiltration of bupivacaine hydrochloride upon pulmonary functions, atelectasis and narcotic need following elective cholecystectomy. *Surgery, Gynecology and Obstetrics* 1983; **157**: 338-40.
- HASHEMI K, MIDDLETON MD. Subcutaneous bupivacaine for postoperative analgesia after herniorrhaphy. *Annals of the Royal College of Surgeons of England* 1983; **65**: 38-9.
- MAY AE, WANDLESS J, JAMES RH. Analgesia for circumcision in children. A comparison of caudal bupivacaine and intramuscular buprenorphine. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 331-3.
- VATER M, WANDLESS J. Caudal or dorsal nerve block? A comparison of two local anaesthetic techniques for postoperative analgesia following day case circumcision. *Acta Anaesthesiologica Scandinavica* 1985; **29**: 175-9.
- MATHER L, MACKIE J. The incidence of postoperative pain in children. *Pain* 1983; **15**: 271-82.
- KAY B. Caudal block for post-operative pain relief in children. *Anaesthesia* 1974; **29**: 610-4.
- LUNN JN. Postoperative analgesia after circumcision. A randomised comparison between caudal analgesia and intramuscular morphine in boys. *Anaesthesia* 1979; **34**: 552-4.
- HAIN WR. Anaesthetic doses for extradural anaesthesia in children. *British Journal of Anaesthesia* 1978; **50**: 303.
- SCHULTE-STEINBERG O, RAHLFS VW. Spread of extradural analgesia following caudal injection in children. A statistical study. *British Journal of Anaesthesia* 1977; **49**: 1027-33.
- ECOFFEY C, DESPARMET J, MAURY M, BERDEAUX A, GIUDICELLI J-F, SAINT-MAURICE C. Bupivacaine in children: pharmacokinetics following caudal anaesthesia. *Anesthesiology* 1985; **63**: 447-8.
- SIMPSON BRJ, PARKHOUSE J. The problem of postoperative pain. *British Journal of Anaesthesia* 1961; **33**: 336-44.
- GERWIG WH, THOMPSON CW, BLADES B. Pain control following upper abdominal operations. *Archives of Surgery* 1951; **62**: 678-82.
- MURRIN KR, ROSEN M. Pain measurement. In: SMITH G, COVINO BG, eds. *Acute pain*. London: Butterworths, 1985: 104-32.
- OWENS ME. Pain in infancy: conceptual and methodological issues. *Pain* 1984; **20**: 213-30.
- YEOMAN PM, COOKE R, HAIN WR. Penile block for circumcision? A comparison with caudal blockade. *Anaesthesia* 1983; **38**: 862-6.

A comparison of midazolam and temazepam for premedication of day case patients

J. J. NIGHTINGALE AND J. NORMAN

Summary

One hundred patients who underwent day case surgery took part in a randomised double-blind comparison between midazolam 15 mg and temazepam 20 mg orally as premedicants. Postoperative recovery was studied using tests of psychomotor function. Midazolam produced a similar degree of anxiolysis to temazepam and a greater incidence of drowsiness. Recovery was similar after either premedicant and psychomotor function was still depressed 4 hours postoperatively ($p < 0.001$). Nearly 90% of patients felt that they had benefitted from either premedicant. We conclude that midazolam is a suitable drug for premedication in day case surgery.

Key words

Anaesthesia; outpatient.

Premedication, benzodiazepines; midazolam, temazepam.

The need for premedication in day case patients remains controversial. Nevertheless, many patients experience considerable anxiety. Drugs with a short elimination half-life are preferred for day case patients. Of the benzodiazepines currently available for oral administration, temazepam has one of the shortest half-lives.¹

Midazolam, a 1,4-imidazo-benzodiazepine, is absorbed rapidly when given orally; peak plasma concentrations are reached within 45 minutes.² It is also eliminated rapidly, with a terminal half-life of approximately 1.75 hours.²

In this study, we compared the efficacy of midazolam and temazepam given orally as premedication in patients undergoing day case surgery. The postoperative effects were also studied.

Methods

One hundred patients scheduled as day cases for excision biopsy of breast lumps, were studied. Their ages ranged from 18 to 65 years and they were classified as ASA grade 1 or 2. No patient was studied who had taken any psychotropic medication within the previous 72 hours or who was taking cimetidine. No patient had cardiopulmonary, hepatic or renal disease. Each patient gave informed consent to the study, which was approved by the hospital ethical committee.

Patients were admitted in the morning for anaesthesia in the afternoon. Approximately 1 hour before surgery, each patient was given a tablet and a capsule and swallowed

these with a small amount of water. Each patient received either temazepam 20 mg or midazolam 15 mg, and a placebo. Neither the patient nor the anaesthetist knew which active medication was given.

Anaesthesia was induced with thiopentone 4 mg/kg and maintained with nitrous oxide 70% and enflurane 1–3% in oxygen. Analgesia after operation comprised two tablets of dispersible aspirin 500 mg and codeine phosphate 8 mg; pethidine 1 mg/kg was given if an opioid was needed. Domperidone 10 mg intramuscularly was given if an antiemetic was required.

The effects of the premedication and anaesthesia were assessed by one of the authors (J.J.N.). Each patient was seen before premedication, one hour after premedication, one hour after operation and 6 hours after premedication (i.e. approximately 4 hours postoperatively). An assessment was made by the anaesthetist of anxiety and sedation at each visit (Table 1).

Table 1. Sedation and anxiety scores.

Score	Sedation	Anxiety
0	Wide awake	Calm
1	Drowsy	Slightly anxious
2	Asleep but rousable	Moderately anxious
3	Unrousable	Very anxious

The patient was asked to undertake two tests of psychomotor function at each visit. The critical flicker fusion threshold (CFFT)³ was determined. This is the average of

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the frequency at which flicker is observed to disappear as the rate increases, and to appear as the rate decreases. A letter cancellation task (LCT) was also completed. Both tests are claimed to detect the effects of low degrees of sedation.^{4,5} Systolic arterial pressure and heart rate were recorded at each visit. Patients were given questionnaires to complete on the first postoperative day. Statistical methods employed were repeated measures analysis of variance or Chi-square tests as appropriate.

Results

The ages and weights of patients in the two groups were comparable (Table 2). The mean durations of anaesthesia

Table 2. Demographic data. Values expressed as mean (SD).

	Midazolam	Temazepam
Age, years	35.2 (10.4)	36.5 (10.8)
Weight, kg	60.0 (9.7)	58.0 (15.0)

were 25.0 minutes (midazolam) and 25.2 minutes (temazepam). Two operations were cancelled and the postoperative data refer to only 98 patients. Three patients in the midazolam group and six in the temazepam group required pethidine postoperatively, and one patient from each group received domperidone.

The anxiety scores are shown in Table 3. It is apparent that there was a marked decrease in the number of patients in each group who displayed anxiety after premedication ($p < 0.001$) but there was no difference between the drugs. Two patients in the midazolam group were unrousable one

Table 3. Anxiety scores: numbers of patients.

	Calm	Slightly anxious	Moderately or very anxious
Before premedication			
Midazolam	30	15	5
Temazepam	30	14	6
1 hour after premedication			
Midazolam	43	4	1
Temazepam	40	9	1
1 hour after surgery			
Midazolam	42	3	1
Temazepam	45	3	0
6 hours after premedication			
Midazolam	47	1	0
Temazepam	49	1	0

Table 4. Sedation scores: numbers of patients.

	Wide awake	Drowsy	Asleep but rousable	Unrousable
Before premedication				
Midazolam	49	1	0	0
Temazepam	50	0	0	0
1 hour after premedication				
Midazolam	23	18	7	2
Temazepam	23	26	1	0
1 hour after surgery				
Midazolam	15	18	13	2
Temazepam	22	18	8	2
6 hours after premedication				
Midazolam	45	1	2	0
Temazepam	44	4	2	0

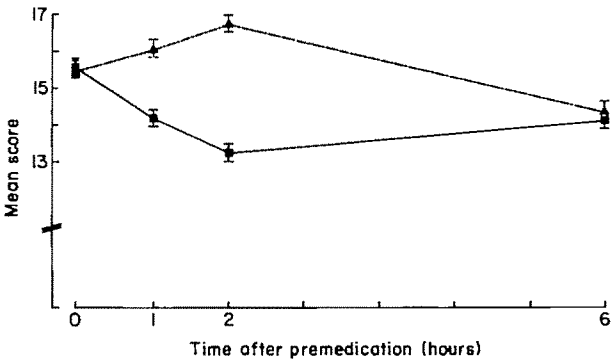


Fig. 1. Mean letter cancellation scores up to 6 hours after premedication with midazolam 15 mg or temazepam 20 mg. Bars represent SEM. ■, midazolam; ▲, temazepam.

hour after premedication, as were two patients in each group one hour after surgery. The anxiety scores for these patients are therefore missing from Table 3.

There was an increase in drowsiness one hour after premedication in both groups (Table 4). Nine patients in the midazolam group were asleep at this time, compared with one in the temazepam group ($p = 0.02$).

Letter cancellation scores are shown in Fig. 1. There was a decrease in performance after midazolam premedication and a further decrease after anaesthesia, with some recovery postoperatively. In contrast, there were improvements in performance after premedication and anaesthesia in the temazepam group. The difference between groups in the pattern of response was significant ($p < 0.001$).

Critical flicker fusion thresholds are displayed in Fig. 2.

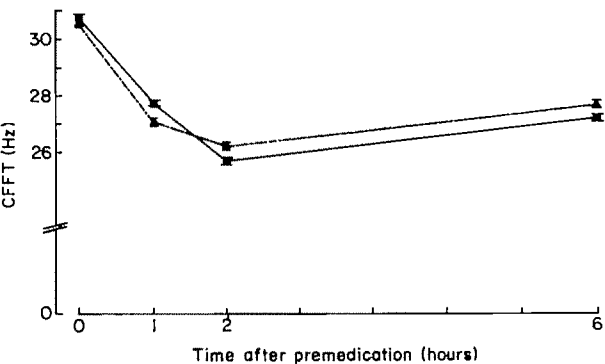


Fig. 2. Mean critical flicker fusion threshold (CFFT) up to 6 hours after premedication with midazolam 15 mg or temazepam 20 mg. Bars represent SEM. ■, Midazolam; ▲, temazepam.

There was a significant ($p < 0.001$) change with time and the trend was very similar in both groups. The CFFT decreased after premedication and again after anaesthesia. It had increased 6 hours after premedication but had not returned to the baseline value.

Questionnaires were returned by 46 patients who received midazolam and 48 who received temazepam. Thirty-six (78%) of the midazolam patients and 39 (81%) of temazepam patients were well enough to return home by 20:00 hours after surgery in the afternoon. Forty patients (86%) who received midazolam and 43 (90%) who received temazepam considered that premedication had been helpful. There were no significant differences between the drugs in these respects.

Discussion

Temazepam has a short elimination half-life with no active metabolites apart from a small amount of oxazepam,¹ and is a satisfactory premedicant for day case surgery.⁶ We have shown that midazolam 15 mg and temazepam 20 mg produce a similar anxiolytic effect, as assessed subjectively by the patient and anaesthetist. Midazolam in this dosage appears to produce significantly greater drowsiness than temazepam.

The improvement in letter cancellation performance after temazepam premedication was an unexpected finding. It is unlikely to be a learning effect, since practice runs were undertaken by all patients and no two letter cancellation forms were the same. It may be a real improvement, or an artifact caused perhaps by the letter cancellation test performed after premedication being easier than the initial version. The decrease in performance with midazolam was probably due to the greater somnolence produced by this sedative. However, the disparity between groups was even larger after anaesthesia; we cannot offer an explanation for this difference. Six hours after premedication, the performance of both groups was close to baseline.

Critical flicker fusion threshold data showed no difference between groups; successive decreases in CFFT occurred after premedication and surgery, with a subsequent return towards normal. Six hours after premedication, mean CFFT remained below baseline value by 3.7 Hz in the midazolam group and 3.0 Hz in the temazepam group. This deficit resulted from the combination of premedicant and anaesthetic agents and confirms the usefulness of CFFT in the detection of residual effects of these drugs in the postoperative period.

Midazolam is not currently available for oral administration. Our study suggests that this preparation confers similar benefits to temazepam, and is an appropriate premedicant for day case surgical patients.

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References

1. FUCCELLA LM, BOLCIONI G, TAMASSIA V, FARRARIO L, TOGNONI G. Human pharmacokinetics and bioavailability of temazepam administered in soft gelatin capsules. *European Journal of Clinical Pharmacology* 1977; **12**: 383-6.
2. SMITH MT, EADIE MJ, BROPHY TO. The pharmacokinetics of midazolam in man. *European Journal of Clinical Pharmacology* 1981; **19**: 271-8.
3. TURNER P. Critical flicker frequency and centrally-acting drugs. *British Journal of Ophthalmology* 1968; **52**: 245-50.
4. HINDMARCH I. Psychomotor function and psychoactive drugs. *British Journal of Clinical Pharmacology* 1980; **10**: 189-209.
5. SMITH JM, MISIAK H. Critical flicker frequency (CFF) and psychotropic drugs in normal human subjects—a review. *Psychopharmacology* 1976; **47**: 175-82.
6. BEECHY APG, ELTRINGHAM RJ, STUDD C. Temazepam as premedication in day surgery. *Anaesthesia* 1981; **36**: 10-15.

Changes in memory following general or spinal anaesthesia for hip arthroplasty

D. HUGHES, J.B. BOWES AND M. W. BROWN

Summary

Patients scheduled for hip arthroplasty were anaesthetised using either general or spinal anaesthesia. Each patient's memory was tested for both recall and recognition by using lists of 10 words each of a different category. This testing for memory extended from the pre-operative visit to one week after operation. Memory was not tested on the day of operation. There was little overall change of memory after either spinal or general anaesthesia although there was an inexplicable but significant decrease in the ability to recognise words after spinal anaesthesia.

Key words

Anaesthetic techniques; inhalational, spinal.

Complications; memory impairment.

Hip replacement is now a standard surgical operation but controversy remains about the relative advantages and disadvantages of general anaesthesia and regional analgesia for this procedure. The discussion includes anxieties about the effects of anaesthesia upon the mental function of an elderly population. Several decades ago there was an alarming report¹ which suggested a deleterious effect of general anaesthesia on the elderly patient. However, a study by Simpson *et al.*² found that the effects on patients submitted for general anaesthesia for elective surgery were minimal. There have been several investigations since then into mental function following anaesthesia.^{3,4} The present study was designed to examine the effects of general anaesthesia or spinal analgesia on memory, a mental function often assumed to be particularly vulnerable to deterioration in the elderly patient.

Methods

Thirty patients among those scheduled for routine cemented hip arthroplasty, were selected for this study on the day before surgery. The patients were between the ages of 50 and 80 years and in ASA classes 1 or 2. Patients who were deaf, those who found writing difficult due to rheumatoid arthritis, and those who appeared to find it difficult to understand the procedure, were excluded. The operations were carried out by one of three consultant surgeons, who used a standard posterior approach to the hip with the

patient in the lateral position; revisions and other more complicated forms of arthroplasty were excluded. The allocation of patients into each of the two groups was arbitrary and there appeared to be little difference between them in respect of surgical technique. The blood loss in each patient was 500–1000 ml and 1 or 2 units of blood were usually transfused.

Details of anaesthesia

Oral temazepam 20 mg was given approximately 2 hours before operation. It was intended that one author (J.B.) would use general anaesthesia, and another (D.H.) would perform spinal anaesthesia; allocation of each patient to one or other group depended upon which consultant surgeon was scheduled to operate, since the two anaesthetists remained with their respective surgeon. In order to balance the numbers at the end of the series, some operations were performed under general anaesthesia administered by D.H.

Patients scheduled for general anaesthesia ($n = 15$) were given thiopentone 250 mg and suxamethonium 70 mg; the trachea was intubated with a 9.5-mm tracheal tube in males, or a 9- or 8.5-mm tube in females. Neuromuscular blockade was continued with alcuronium 20 mg, and pentazocine 60 mg was given for analgesia. Anaesthesia was maintained with nitrous oxide in 30% oxygen and 0.5% halothane, and the lungs were ventilated with either a Manley or Penlon ventilator, using a minute volume of 100 ml/kg.

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Patients scheduled for spinal analgesia ($n = 15$) were given minimal sedation (2.5–5 mg midazolam). Spinal analgesia was administered through a 22-gauge needle in the midline of the L_{3/4} interspace, with the patient in the lateral decubitus position. A single dose of 2–4 ml bupivacaine 0.5% was injected without barbotage. The patient's interest in the surgery was diverted by music. Deliberate hypotension was not used; if necessary, the systolic blood pressure was maintained above 85 mmHg by using vasopressors.

The experimental procedure was explained during the pre-operative visit and patients were asked to give verbal consent; permission to carry out the study with only verbal consent was obtained from the district ethical committee. The patients were then fitted with earphones connected to a tape cassette before they were given a card that contained 10 words belonging to a single category, such as insects.^{5,6} Obvious sexual bias was avoided by balancing the categories, e.g. weapons and kitchen utensils. In addition to the visual input from the cards, the headphones were used to relay a male voice that read the 10 words at the rate of one word per second (audible input). A random sequence of six digits was given from the tape recorder at the end of the category list of 10 words, but without visual input of the number. This number, which was given to block the recency effect, was not scored. The patient was asked to write down the number as soon as it was given, followed by as many of the category words as possible, in any order.

Four lists of words were presented in the recall test for new material during the pre-operative visit. There was a gap of a few minutes after the fourth list before the cards of the first and second category lists were shown again. The material of one of these cards was used for a further recall test (repeat recall test) using the same protocol as for the initial test; the other card was used for a recognition test. In this recognition test, the patient was given a card containing 20 words all from the same category. The patient was asked to write down the 10 words from this card which had been presented previously.

The patients were tested for their recall of two lists of new material during subsequent visits in the postoperative period. One of the lists of words which had been presented at the previous visit was re-presented and used for the repeat recall test, whilst the other list was re-presented and used for a recognition test. The order of testing of recall or recognition was randomised across lists and patients. The full protocol is shown in Table 1. The written answers for either recall or recognition for each category list were

scored to a maximum of 10; no marks were deducted for incorrect answers. False positives in the recall tests were rare.

The main objective was to compare the effects of two types of anaesthesia on memory, so the averages of the recall scores of each patient for the lists of new material presented during the postoperative period (at 24 hours, 48 hours and one week) were subtracted from the averages for the four lists of new material presented before operation. The average differences, before minus after operation, reflect any change in results for the tests performed at the various times postoperatively. The data were analysed by a nested (split-plot) analysis of variance with the effect of type of anaesthesia tested between subjects in the two groups, and the effect of time after the operation and the interaction between this time and the type of anaesthesia tested within the subjects.

Results

The mean ages of the patients were 69 years in the spinal group and 67 years in those who received general anaesthesia. Figure 1 shows the percentage recall of newly pre-

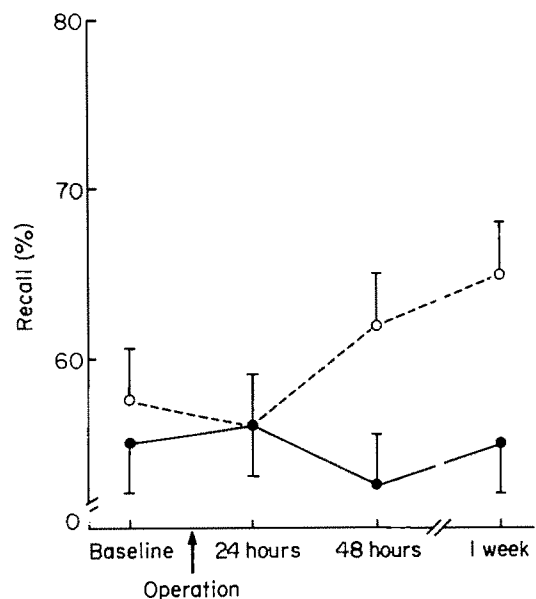


Fig. 1. Mean (SD) percentage recall of newly presented material before and after hip arthroplasty conducted under general (○, $n = 15$) or spinal (●, $n = 15$) anaesthesia.

sented material, which was not affected significantly in either group at any time after operation. There was no difference (independent t -test, $p > 0.05$) between groups in respect of the results of the pre-operative tests.

Figure 2 shows the results of the repeat recall and recognition tests which were analysed in the same way, by calculating the before minus after, in scores for each patient for each postoperative time of testing. Analysis of variance for the repeat recall data indicated a significant decrease in performance from the pre-operative test to the postoperative period ($p < 0.01$), but there was no significant difference in respect of the type of anaesthesia, or of the interaction between time and type of anaesthesia.

It should be noted from Figs. 1 and 2 that the pre-operative test was the only one which showed any marked improvement in the score for the repeat test compared to the first

Table 1. Experimental protocol.

	New material (recall)	Old material (repeat recall and recognition)
Pre-operative	XA/BC	XA
24 hours postoperative	DE	BC
48 hours postoperative	FG	DE
1 week postoperative	HI	FG

The categories were: X, articles of clothing; A, occupations; B, parts of a building; C, weapons; D, kitchen utensils; E, birds; F, furniture; G, musical instruments; H, fruits; I, flowers. X was originally considered to be expendable and was designed to give the patients practice with the procedures. However, results for this list did not differ significantly from those of the other pre-operative lists and so were included in the analysis.

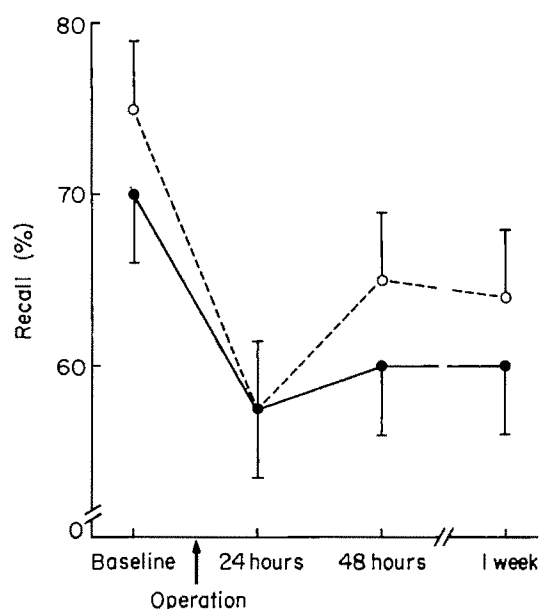


Fig. 2. Mean (SD) percentage recall of previously presented material (repeat recall test) before and after hip arthroplasty conducted under general (○, $n = 15$) or spinal (●, $n = 15$) anaesthesia.

test. The time between the first and second presentations of the lists was only a few minutes at the pre-operative test, but 24 hours or longer for all the postoperative tests. Both groups performed worst in relation to the material first presented pre-operatively and re-presented and tested 24 hours after operation. At 24 hours, the performance of the group that received general anaesthesia was significantly worse ($p < 0.05$) than that at 48 hours or one week after operation.

Figure 3 shows the results of repeat recognition, which

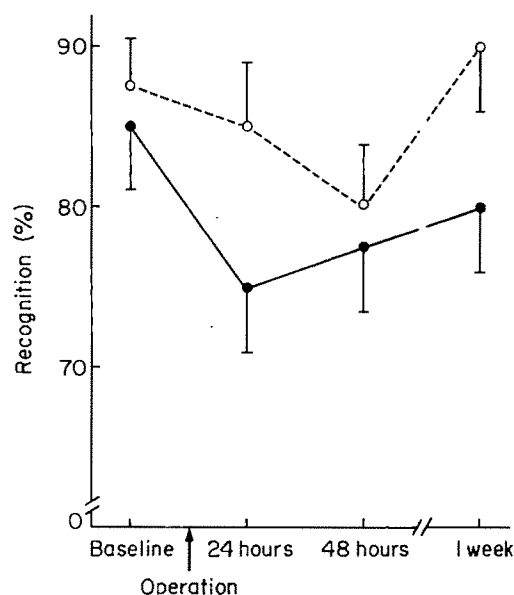


Fig. 3. Mean (SD) percentage recognition of previously presented material before and after hip arthroplasty conducted under general (○, $n = 15$) or spinal (●, $n = 15$) anaesthesia.

again involved material which was presented twice. There were significant ($p < 0.05$) effects from the type of anaesthesia and the time of testing, but no significant interaction between them for the before minus after differ-

ences. Thus the overall performance of the spinal group was significantly worse after operation than that of the general anaesthesia group. The before minus after difference for the spinal group was significantly ($p < 0.05$) greater than that for the general anaesthesia group at 24 hours; the difference between groups one week after operation was not statistically significant ($0.10 > p > 0.05$).

The spinal group performed worst 24 hours after operation but the general anaesthesia group was worst at 48 hours. The two treatment groups were well matched in their performance before operation.

Discussion

A recent editorial⁷ highlighted the widespread interest in the relationship between memory and anaesthesia. The particular interest of that article was the possible relationship between awareness and memory during anaesthesia. It has been suggested that anaesthesia blocks retrieval rather than input or encoding of memory.

The other interest in memory during anaesthesia relates to the fear that the overall effects of surgery might diminish memory in an elderly population. The overall effects of surgery include not only anaesthesia and the endocrine effects of surgery but also the removal of the patient from his surroundings. Several decades ago this was shown to be particularly harmful to the patient if the operation was an emergency,¹ although for the elective surgical operation the effects appear to be minimal.² A more recent article⁸ compared mental function before and after surgery for fractured neck of femur, and found no significant difference between patients who received general anaesthesia and those who had spinal block.

The present study attempted to apply more sophisticated techniques of memory research to the clinical situation. Most of the memory testing reported previously has consisted of testing for yes/no recognition of simple visual stimuli.⁹ The recall and recognition of word lists after distraction involves the use of long-term episodic memory. Such memory has been shown to be particularly vulnerable to brain insult, and is impaired in the typical organic amnesic syndrome, in dementia of the Alzheimer type and by the administration of some benzodiazepines or hyoscine.^{5,6,10,11} Indeed, lorazepam has been used as a model for the study of dementias.

The testing of mental function in psychology students can be of long duration and considerable sophistication. However, there is a possibility of extraneous stimuli in the clinical situation and patients are likely to display pre-operative anxiety, postoperative discomfort and lack of motivation; consequently, the protocol in this study had to be fairly short. Despite the use of a concise protocol, the study was abandoned for several months because a number of patients who were willing to do the control tests failed to perform the postoperative tests. The loss of these patients, and the fact that some patients for hip arthroplasty were not included in the series because of difficulty in understanding the protocol, may have resulted in a degree of patient selection, although this should not have biased treatment comparisons. However, this inadvertent selection may explain the high level of performance which was recorded, and might possibly account for the absence of serious memory problems. The timing of the tests was designed to investigate any effect that persisted beyond the transient

impairment which might occur in the immediate postoperative period.⁵ The protocol did not extend beyond one week because of administrative difficulties and because it was felt that any permanent deficit of memory would have become apparent by this time.

There was little difference between the spinal and the general anaesthesia groups in respect of recall of data which had not been presented before. Performance of the repeat recall test was better at the pre-operative than at the post-operative visit. This difference is not surprising and cannot be ascribed solely to the operation, since the time between the presentations of the first and repeat tests was only a few minutes compared to 24 hours or more for the post-operative tests.

The significant reduction in postoperative recognition performance is of interest in that it accords with earlier work with lorazepam which suggested that recognition can be more sensitive than free recall to disturbance.^{5,6} The spinal group was more impaired than the general anaesthesia group. However, the difference between the groups is not so great as to give rise to major concern. The results shown in Fig. 3 might suggest that patients benefited so much from the first exposure and recall testing during the pre-operative visit that they were approaching the ceiling for that recognition test. These arguments do not apply for the postoperative testing, since significant differences were found between the two groups. The decrease in performance in both groups at 24 and 48 hours after operation is in agreement with the findings of Bigler *et al.*⁸

The most striking features of the study were the high initial performance of a totally new challenge to the patient in unfamiliar surroundings, and the lack of any major effect on memory of surgery for either type of anaesthesia.

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References

1. BEDFORD PD. Adverse cerebral effects of anaesthesia on old people. *Lancet* 1955; **2**: 259-63.
2. SIMPSON BR, WILLIAMS M, SCOTT JF, CRAMPTON SMITH A. The effects of anaesthesia and elective surgery on old people. *Lancet* 1961; **2**: 887-93.
3. RIIS J, LOMHOLT B, HAXHOLDT D, KEHLET H, VALENTIN N, DANIELSEN U, DYRBERG V. Immediate and long-term mental recovery from general versus epidural anaesthesia in elderly patients. *Acta Anaesthesiologica Scandinavica* 1983; **27**: 44-9.
4. HOLE A, TERJESSEN T, BREVIK H. Epidural versus general anaesthesia for total hip arthroplasty in elderly patients. *Acta Anaesthesiologica Scandinavica* 1980; **24**: 279-87.
5. BROWN J, LEWIS V, BROWN MW, BOWES JB. Amnesic effects of intravenous diazepam and lorazepam. *Experientia* 1978; **34**: 501-2.
6. BROWN J, BROWN MW, BOWES JB. Effects of lorazepam on rate of forgetting, on retrieval from semantic memory and manual dexterity. *Neuropsychologia* 1983; **21**: 501-2.
7. JONES JG, KONIECZKO K. Hearing and memory in anaesthetised patients. *British Medical Journal* 1986; **292**: 1291-3.
8. BIGLER D, ADELHOJ B, PETRING OU, PEDERSON NO, BUSCH P, KAHLKE P. Mental function and morbidity after acute hip surgery during spinal and general anaesthesia. *Anaesthesia* 1985; **40**: 672-6.
9. BETHUNE DW. Test of delayed memory recall suitable for assessing postoperative amnesia. *Anaesthesia* 1981; **36**: 942-8.
10. MORRIS RG, KOPELMAN MD. The memory deficits in Alzheimer-type dementia: a review. *Quarterly Journal of Experimental Psychology* 1986; **38A**: 575-602.
11. SQUIRE LR. Mechanisms of memory. *Science* 1986; **232**: 1612-9.

CASE REPORT

Acute inversion of the uterus at Caesarean section

Implications for the anaesthetist

R. S. EMMOTT AND A. BENNETT

Summary

Two cases of acute inversion of the uterus that occurred through the uterine incision at the time of Caesarean section are described. These represent only the sixth and seventh cases reported in the literature at this time. The implications for the anaesthetist are discussed.

Key words

Anaesthesia, obstetric; Caesarean section.

Complications; hypotension, uterine inversion.

Acute inversion of the uterus following delivery is a rare event, particularly through the uterine incision during Caesarean section; only five cases of the latter have been reported. We report here a further two such cases.

Case histories

Case 1

A healthy, 35-year-old primigravid female at term presented for emergency Caesarean section following the advent of fetal distress. General anaesthesia was induced and a live infant delivered via an incision in the lower uterine segment. Synthetic oxytocin 5 units and papaveretum 20 mg were then administered intravenously and the volatile agent enflurane discontinued. Arterial blood pressure and heart rate remained stable during this period at 110/80 mmHg and 95–105 beats/minute, respectively.

Controlled cord traction was applied shortly afterwards to facilitate placental delivery; complete uterine inversion through the lower segment incision immediately followed. Rapid intravenous infusion of colloid solution was commenced in the expectation of hypotension; arterial blood pressure, however, remained stable initially and only after 20 minutes of inversion did it begin to decrease, reaching 80/60 mmHg. The uterus was eventually re-inverted following spontaneous separation of the placenta; inversion to re-inversion time was 40 minutes. No further oxytocic agent was administered. Haemodynamic status improved immediately and arterial pressure remained at 110/80–120/85 mmHg until the end of the procedure. At no time was bleeding thought to be excessive and total blood loss

was estimated to be 800 ml. Polygeline solution 1000 ml and Hartmann's solution 500 ml were administered during the period of inversion. No adverse postpartum sequelae occurred.

Case 2

A healthy, 31-year-old para 1 + 0 woman at 41 weeks' gestation presented for emergency Caesarean section because of failure to progress in the first stage of labour. Epidural anaesthesia had been employed successfully up to this point; a further 10 ml bupivacaine 0.5% was given and provided satisfactory blockade for the proposed procedure. A live infant was delivered by lower segment Caesarean section. Synthetic oxytocin 10 units was given intravenously, together with droperidol 2.5 mg to treat mild maternal nausea. Arterial blood pressure and heart rate remained stable at 140/90 mmHg and 80–100 beats/minute, respectively, throughout this period.

Spontaneous inversion of the uterus through the lower segment incision occurred 2 minutes after delivery. A fundally situated placenta remained firmly adherent to the uterus. Only after a further 25 minutes did attempts at placental removal and uterine re-inversion prove successful. A further 10 units of synthetic oxytocin were then administered by bolus intravenous injection. The patient remained remarkably comfortable during the whole period of inversion; blood loss was not excessive and arterial pressure and heart rate remained stable at pre-delivery levels. Polygeline solution 1000 ml was administered intravenously during this period.

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The patient became pale, sweaty and distressed 5 minutes after uterine re-inversion, without further overt bleeding, and complained of chest tightness. Arterial pressure decreased rapidly to 70/40 mmHg and the heart rate increased to 130 beats/minute. A high concentration of oxygen was given by facemask and ephedrine 10 mg administered intravenously in divided doses. Rapid blood transfusion was commenced, followed by further colloid solution. The chest symptoms disappeared rapidly but hypotension (systolic arterial pressure below 100 mmHg) resolved only gradually over the next 20 minutes. Surgery was concluded without further incident; blood loss in total was approximately 700 ml. No adverse postpartum sequelae were observed except heavy lochia. Her haemoglobin level 24 hours postoperatively was 9.5 g/dl compared to the pre-operative value of 11.6 g/dl.

Discussion

Acute uterine inversion is a rare phenomenon and most commonly occurs *per vaginam*. The cardinal features of acute inversion *per vaginam* are abdominal pain, haemorrhage, shock and a vaginal mass. Shock is often profound and of rapid onset; its degree may be out of proportion to the extent of blood loss.^{1,2} Average blood loss has been quoted as 1775 ml.³ The possible mechanisms of shock include haemorrhage, stretching of the broad ligaments and peritoneum, and ovarian compression.¹ A review of the literature reveals no report in which the presence of regional blockade has been thought to influence the degree of haemorrhage or shock. Rapid treatment of the inversion and its haemodynamic sequelae is associated with decreased maternal morbidity¹ and mortality.²

Inversion of the uterus during Caesarean section is extremely rare and only five previous cases have been reported.⁴⁻⁷ In all cases inversion occurred shortly after delivery of the infant, and in four of the five cases, before delivery of the placenta. Inversion in three instances immediately followed uterine contraction secondary to oxytocin administration. It is interesting that no report identifies haemorrhage as a feature of uterine inversion during Caesarean section; indeed, in only one case is hypotension commented upon. The decrease in arterial blood pressure described by the author as 'quite remarkable', was apparently readily reversed on uterine re-inversion.⁴ Re-inversion was apparently achieved easily in all cases except that associated with hypotension. No serious sequelae were encountered in any case.

Our two reported cases do share some features in common with those reported previously. A common observation is the absence of excessive bleeding; in this respect uterine inversion at Caesarean section does seem to differ from acute inversion *per vaginam*, where haemorrhage is reported to occur in 68%² to 94%³ of cases. Inversion in both cases occurred before placental separation and was temporally related to the administration of an oxytocic agent, as in most previous reports. The major differences between our cases and those previously reported, are the prolonged inversion to re-inversion time and, notably, acute hypotension on uterine re-inversion in case 2. Haemodynamic instability in both cases appeared to be out of proportion to the degree of blood loss and occurred despite significant intravenous fluid therapy.

The advent of haemodynamic instability in the absence of significant haemorrhage, implies that other hypotensive factors are operating. It is therefore likely that effects secondary to peritoneal and broad ligament stretching and ovarian compression are important in the genesis of hypotension associated with uterine inversion at Caesarean section. Whatever the effector mechanism, visceral afferent autonomic nerves associated with lower thoracic, upper lumbar and sacral spinal levels are presumably involved in afferent pathways. High epidural block would be expected to obtund these afferents at spinal level and therefore prevent the hypotensive response; this may explain the absence of hypotension during the period of uterine inversion in case 2. General anaesthesia also obtunds afferent transmission at spinal level to a degree that depends on depth of anaesthesia. Light or lightening anaesthesia may explain the delayed onset of hypotension in case 1.

The acute onset of hypotension in case 2 is more difficult to explain; re-inversion of the uterus usually improves haemodynamic status in acute inversion *per vaginam*. The following is a speculative explanation of the events that led to hypotension on uterine inversion in this case. It is known that uterovenous compression may be associated with uterine inversion and may contribute to venous haemorrhage.⁸ Uterovenous compression may result in the accumulation of metabolic products in the uterine tissues; the degree of accumulation depends upon the degree of uterovenous compression, the duration of inversion and, in the absence of venous haemorrhage, the degree of arterial inflow obstruction. Uterine re-inversion, with restoration of uterine circulation following prolonged inversion, could therefore be associated with a sudden release of these metabolic products into the general circulation; their vasodilator effects might then cause acute hypotension. Concurrent administration of a vasodilator drug such as synthetic oxytocin, which was given on re-inversion in this case but not in case 1, would exacerbate the hypotension. Epidural blockade may also have been a contributory factor, because of impairment of compensatory mechanisms during hypovolaemia.

In conclusion, acute inversion of the uterus during Caesarean section is extremely rare. Delay in re-inversion may be associated with hypotension despite rapid intravenous fluid therapy; delay should be minimised by re-inverting the uterus with the placenta still attached if placental separation has not occurred. It is possible that the presence of regional blockade may prevent hypotension during the period of inversion. No oxytocic agent should be administered while the uterus is inverted, because the resulting increase in uterine tone will severely impede attempts at re-inversion in the short term. If inversion occurs in a patient under general anaesthesia and bleeding is not excessive, increasing the depth of anaesthesia with a volatile inhalational agent will relax uterine tone and facilitate re-inversion and may, paradoxically, prevent hypotension. In an awake patient undergoing Caesarean section under regional anaesthesia, uterine relaxation may be brought about with terbutaline⁹ or ritodrine¹⁰ intravenously, or amyl nitrate inhalation. Synthetic oxytocin will increase uterine tone, reduce uterine bleeding and help to prevent recurrent inversion once the uterus has been successfully re-inverted; however, it should be administered with caution and certainly not as an intravenous bolus injection. Prolonged inversion may be associated with

hypotension following re-inversion even (or perhaps especially) in the presence of regional blockade.

Acknowledgment

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References

1. KITCHEN JD, THIAGARAJAH S, MAY HV, THORNTON WN. Puerperal inversion of the uterus. *American Journal of Obstetrics and Gynecology* 1975; **123**: 51-8.
2. BELL JE, WILSON GF, WILSON LA. Puerperal inversion of the uterus. *American Journal of Obstetrics and Gynecology* 1953; **66**: 767-77.
3. WATSON P, BESCH N, BOWES WA. Management of acute and subacute puerperal inversion of the uterus. *Obstetrics and Gynecology* 1980; **55**: 12-16.
4. DONALD I. *Practical obstetric problems*, 5th edn. London: Lloyd Luke Ltd, 1979: 804-11.
5. DAVIS GH. Acute inversion of the uterus, with a report of four cases. *American Journal of Obstetrics and Gynecology* 1933; **26**: 249-54.
6. KALTREIDER DF, WEST GB. Acute puerperal inversion of the uterus, with 2 cases seen at Cesarean section. *Bulletin of the School of Medicine of the University of Maryland* 1946; **31**: 144-50.
7. LOIZEAUX LS, MASTRAIOINNI L. Acute puerperal inversion of the uterus; review of 10 years experience; report of 4 cases. *Obstetrics and Gynecology* 1955; **5**: 193-7.
8. CRAWFORD JS. *Principles and practice of obstetric anaesthesia*, 5th edn. Oxford: Blackwell Scientific Publications, 1984: 346.
9. KOVACS BW, DE VORE GR. Management of acute and subacute puerperal uterine inversion with terbutaline sulfate. *American Journal of Obstetrics and Gynecology* 1984; **150**: 784-6.
10. CLARK SL. Use of ritodrine in uterine inversion. *American Journal of Obstetrics and Gynecology* 1985; **151**: 705.

CASE REPORT

Fibreoptic bronchoscopic nasotracheal intubation of a neonate with Pierre Robin syndrome

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Summary

A case of nasotracheal intubation using a fibreoptic bronchoscope and the Seldinger technique is described. A guide wire was passed through the suction channel of the fibroscope after the epiglottis and the vocal cords were seen; the fibroscope was removed and a nasotracheal tube passed over the wire into the trachea.

Key words

Intubation, tracheal.

Complications; Pierre Robin syndrome.

Tracheal intubation of children with the Pierre Robin and related syndromes is often very difficult.^{1–3} Various methods have been proposed to solve the problem of difficult paediatric intubation: blind nasotracheal intubation with or without a stylet,⁴ blind nasotracheal intubation using the fingers to guide the tube into the trachea,¹ blind nasotracheal intubation in the prone position,⁵ a retrograde technique using a guide wire,⁶ direct laryngoscopy and pulling out the tongue,³ tracheotomy² and, in larger children, fibreoptic bronchoscopic intubation.^{7,8} Fibreoptic bronchoscopic intubation of very small children is usually thought to be impossible^{4,7,8} but a two-stage fibre-bronchoscopic approach was recently reported.⁹ We present a method of fibreoptic nasotracheal intubation of small infants based on the Seldinger principle.¹⁰

Case history

A 3-day-old, 3.3-kg male infant was transferred from a local hospital because of oesophageal atresia. The infant had the Pierre Robin syndrome with severe micrognathia, macroglossia and a wide cleft palate. A resection and anastomosis of the oesophagus was planned. Premedication consisted of intramuscular atropine 0.03 mg. Direct laryngoscopy was attempted after intramuscular ketamine 25 mg but neither the larynx nor the epiglottis could be seen. It was therefore decided to try a fibreoptic nasotracheal intubation.

The nasal cavity and pharynx were sprayed with lignocaine. The flexible fibreoptic bronchoscope (Olympus BF3 C4, 3.6 mm outer diameter, 60 cm long, 1.2 mm suction

channel) was passed through the right nostril while an assistant held the tongue with Magill forceps, and the epiglottis and the vocal cords were easily seen. A teflon-coated guide wire (150 cm long, 0.9 mm diameter) with a flexible tip was passed through the suction channel and inserted under direct vision through the laryngeal orifice into the trachea until a slight resistance was felt. The fibroscope was carefully removed and a 3 mm nasotracheal tube passed over the wire into the trachea without difficulty. The duration of the intubation procedure was 7 minutes. Extubation 2 days later was uneventful.

Discussion

Fibreoptic bronchoscopic techniques have been used increasingly during the past 5–7 years for difficult paediatric intubation.^{7,8,11} However, 'over-the-scope' tracheal intubation can be used only for children older than 18 months, because of the relatively large diameter of the fibrebronchoscope.⁷ In 1974, Stiles¹⁰ advocated the use of a flexible wire passed through the suction channel of the fibrebronchoscope as a guide for the tracheal tube. This method is now, with the appearance of small diameter fibreoptic bronchoscopes, applicable for intubation of small infants. Stiles reinforced the guide wire with a cardiac catheter before the tracheal tube was finally placed. This double manipulation may increase the risk of displacement of the guide wire. We believe that the use of a flexible guide wire without a stiffening cardiac catheter reduces the time required for intubation and does not increase the risk of displacement of the tracheal tube into the oesophagus.

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Different modifications of the technique must be used depending on the diameter of the trachea.^{1,2} The tip of the fibrebronchoscope cannot enter the trachea in premature and newborn infants (tube 2–3 mm) without severely interfering with spontaneous ventilation; consequently, the tip of the fibrebronchoscope is stopped before it enters the trachea and the guide wire inserted into the trachea under direct vision. The diameter of the trachea in infants who need a tube of 3–4 mm allows passage of the fibrebronchoscope and the guide wire can be advanced further under direct vision. The usual 'tube-over-the-scope' method can be used in children whose tracheal diameter allows the passage of tubes of 4.5 mm or more.

A few technical points must be emphasised, because they may mean the difference between success and failure. Pre-medication should include atropine to prevent excessive upper airway secretion. Sedation (for instance with ketamine) and local analgesia should be employed to preserve spontaneous ventilation and the tone of the pharyngeal musculature. The tube should be withdrawn by 0.5–1 cm and rotated 90–180° before it is advanced again if resistance is encountered when it reaches the larynx.

The method has only a few drawbacks. Suitable fibreoptic bronchoscopes are expensive, and the position of the tracheal tube cannot be confirmed visually. We consider that the method employed is fast, reliable and non-traumatic, but it does require experience in the use of fibreoptic bronchoscopes.

References

1. SKLAR GS, KING BD. Endotracheal intubation and Treacher–Collins syndrome. *Anesthesiology* 1976; **44**: 247–9.
2. DYKES EH, RAINE PAM, ARTHUR DS, DRAINER IK, YOUNG DG. Pierre Robin syndrome and pulmonary hypertension. *Journal of Pediatric Surgery* 1985; **20**: 49–52.
3. MIYABE M, DOHI S, HOMMA E. Tracheal intubation in an infant with Treacher–Collins syndrome—pulling out the tongue by forceps. *Anesthesiology* 1985; **62**: 213–4.
4. BERRY FA. The use of a stylet in blind nasotracheal intubation. *Anesthesiology* 1984; **61**: 469–71.
5. POPULAIRE C, LUNDI JN, PINAUD M, SOURON R. Elective tracheal intubation in the prone position for a neonate with Pierre Robin syndrome. *Anesthesiology* 1985; **62**: 214–5.
6. BORLAND LM, SWAN DM, LEFF S. Difficult pediatric endotracheal intubation: a new approach to the retrograde technique. *Anesthesiology* 1981; **55**: 577–8.
7. RUCKER RW, SILVA WJ, WORCESTER CC. Fiberoptic bronchoscopic nasotracheal intubation in children. *Chest* 1979; **76**: 56–8.
8. HEMMER D, LEE T-S, WRIGHT BD. Intubation of a child with a cervical spine injury with the aid of a fiberoptic bronchoscope. *Anesthesia and Intensive Care* 1982; **10**: 163–5.
9. BERTHELSEN P, PRYTZ S, JACOBSEN E. Two-stage fiberoptic nasotracheal intubation in infants: a new approach to difficult pediatric intubation. *Anesthesiology* 1985; **63**: 457–8.
10. STILES CM. A flexible fiberoptic bronchoscope for endotracheal intubation of infants. *Anesthesia and Analgesia* 1974; **53**: 1017–9.
11. OVASSAPIAN A, DYKES MHM, YELICH SJ. Difficult pediatric intubation—an induction for the fiberoptic bronchoscope. *Anesthesiology* 1982; **56**: 412–3.
12. LANE GA, PASHLEY NRT, FISHMAN RA. Tracheal and cricoid diameters in the premature infant. *Anesthesiology* 1980; **53**: S326.

CASE REPORT

Penetrating tracheal injury in a child

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Summary

A case is reported of a 3.5-year-old child with a stab wound in the neck, that penetrated the trachea. A pneumomediastinum was present. The anaesthetic problems are discussed and the child's management outlined.

Key words

Anaesthesia; paediatric.

Complications; tracheal injury, pneumomediastinum.

Neck injuries may be associated with penetration of the airway and this can lead to serious thoracic consequences. Rapid surgical repair of such injuries is essential. This may pose anaesthetic problems and a case is reported of such an injury in a young child.

Case history

A previously healthy 3.5-year-old boy who weighed 18 kg was admitted to hospital. He had fallen onto the upturned open blades of a pair of scissors, whereupon he experienced immediate difficulty in breathing and turned blue for a few seconds. However, he was able to breathe easily after an initial bout of coughing, and there was no voice change. He had sustained two puncture wounds in the anterior neck just above the suprasternal notch. Blood loss was minimal although there was slight haemoptysis at first.

His face and neck began to swell immediately and he was taken to the local accident and emergency department. A chest radiograph was taken together with soft-tissue views of the neck. These confirmed surgical emphysema of the neck, together with air in the mediastinum. He was transferred to Whipps Cross Hospital and admitted under the care of the ENT surgeons. The facial and neck swelling were considerably worse by this time.

On examination the boy was quiet but frightened. There was no cyanosis but there was peri-orbital puffiness together with swelling, mainly on the right side of the face and neck, which was clearly emphysematous. There was an obvious air leak through one of the two wounds. The pulse rate was 100 beats/minute and regular. The arterial blood pressure was 100/70 mmHg. The jugular venous pulse could not be seen on either side. There were no added heart

sounds and air entry on both sides of the chest was good; the breath sounds were vesicular.

Blood investigations were normal except for a serum potassium of 3.0 mmol/litre which was treated as soon as the result was available. A further chest radiograph (Fig. 1)

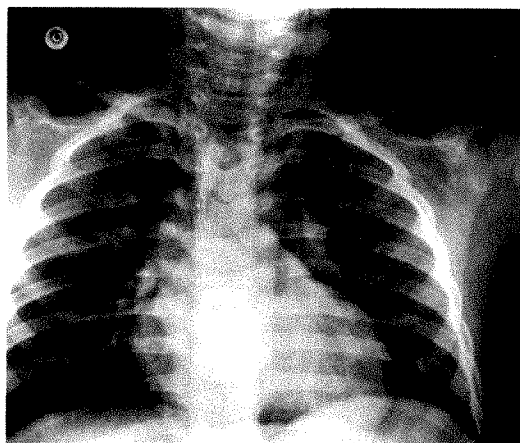


Fig. 1. Postero-anterior chest X ray showing pneumomediastinum and subcutaneous emphysema of the neck.

showed increased surgical emphysema and expansion of the pneumomediastinum and it was decided to proceed to surgery.

The boy had eaten 2 hours before injury, and had drunk water 30 minutes before injury. The anaesthetist was notified 4 hours after injury. The boy had refused all injections and was very anxious. It was considered essential to establish intravenous access and he cooperated with the insertion of a 20-gauge cannula after which 0.9% saline

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was infused at a rate of 100 ml/hour. He was given humidified oxygen via a facemask with FiO_2 0.35. Atropine 0.6 mg was given by mouth and one hour later he was taken to the operating room. Anaesthesia was induced with an ENT surgeon standing by, scrubbed; instruments were available for immediate rigid bronchoscopy and tracheostomy if necessary. A suction system was placed, switched on, under the pillow and the noise minimised to prevent disturbance of the child. The ECG was monitored throughout and a precordial stethoscope attached before induction of anaesthesia.

Anaesthesia was induced with oxygen and halothane, the latter increasing to 4.5%. Much of the fresh gas initially escaped through the tracheal leak. This was sealed temporarily with a polyethylene dressing. This ensured that the fresh gas was inhaled but the surgical emphysema became visibly worse. Tracheal intubation was attempted after the larynx was sprayed with lignocaine. However, the depth of anaesthesia was inadequate and the pulse rate slowed to 80 beats/minute. The polyethylene dressing was removed at this point, and oxygenation by facemask re-established. Atropine 0.3 mg was given intravenously followed by thiopentone 15 mg, and the trachea was intubated successfully with a 5.0-mm uncuffed tracheal tube. The tube was passed deliberately beyond the carina and then withdrawn until inflation of both lungs was confirmed. The tube was taped in place and held by the anaesthetist throughout the procedure. Ventilation was spontaneous, using an Ayre's T-piece system with a Jackson-Rees reservoir bag attached. After intubation, anaesthesia was maintained with oxygen and halothane plus fentanyl 25 μg .

Antitetanus toxoid was given subcutaneously, together with amoxycillin 50 mg. A 4-mm diameter gap was found in the third and fourth tracheal rings and was repaired with proline 4.0×3 sutures. A corrugated drain was inserted and the skin repaired with proline 4.0×5 sutures.

The child's trachea was extubated at the end of the procedure, when his eyes opened to command. There was no difficulty in breathing. He was transferred to the intensive therapy unit, together with tracheal dilators, and a selection of instruments placed ready for emergency establishment of an airway if necessary. Humidified oxygen 35% was again given by facemask for the first 2 hours, but thereafter removed because it was not tolerated.

The intravenous infusion was continued at 50 ml/hour with 4.0% glucose/0.18% saline, to which potassium was added. The facial swelling was much reduced by the next morning. When he drank freely, the intravenous infusion was removed and he was transferred to the paediatric ward. The antibiotics were continued orally.

He paid a visit to the intensive therapy unit on the fourth day. He was unrecognisable, since all the facial swelling had resolved.

Discussion

Neck trauma should always be investigated for possible injury to the airway. The following are particularly indicative:¹ midline injury, dyspnoea, cyanosis, haemoptysis, dysphagia, hoarseness of voice and bubbles in blood lost from wounds. The possibility of impending airway obstruction is suggested by oedema from injury, by haematoma from vascular injury and by subcutaneous emphysema. Actual airway obstruction may be indicated by respiratory

stridor that begins during expiration and progresses into inspiration.

Radiographic investigation is essential in neck injury. Preferably, inspiratory and expiratory chest radiographs and lateral soft-tissue neck views should be obtained. In this way, air leaks within the chest can be identified and the larynx and trachea outlined. No patient should be sent to the X ray department unaccompanied by an anaesthetist, however, since airway obstruction may occur without warning.

Immediate or eventual tracheostomy may be necessary after airway injury. In children, however, this carries the risk of serious sequelae,² such as infection and tracheal stenosis. Oral or nasal tracheal intubation is preferable where possible.

Bronchoscopy is mandatory in a case with possible intrathoracic airway injury or where a foreign body may lie in the airway. Grover³ recommends the use of an intubating bronchoscope followed by a tracheal tube. Immediate thoracotomy is necessary in the case of an intrathoracic airway injury; positive pressure through any tracheal tube may well exacerbate an air leak distal to its tip, until that leak is surgically repaired. However, bronchoscopy is unnecessary with a well-defined cervical tracheal injury and no foreign body, and the airway should be secured with a tracheal tube from the outset.

There are three possible techniques for tracheal intubation of an adult patient with such an injury: awake intubation with topical anaesthesia, inhalational induction of anaesthesia, or rapid sequence induction with thiopentone and suxamethonium. Herrin *et al.*¹ suggest that awake intubation avoids the risk of positive pressure ventilation which might exacerbate an air leak. However, this is not feasible in young children. Brown and Fisk⁴ recommend inhalational induction of general anaesthesia for injuries above the glottis, in order to avoid the use of suxamethonium, which might obstruct the patient's own efforts to maintain an airway. Nitrous oxide must also be avoided in any neck injury since even a normal chest radiograph does not exclude the possibility of an air leak into the chest; any air collection would accumulate nitrous oxide and so expand. As a result, inhalational induction depends upon high inhaled concentrations of volatile anaesthetics, with possible side effects such as vascular dilatation. Haemorrhage or air embolus are possible where blood vessels have been severed, and it is preferable to lie the child flat or even slightly head-down, to reduce the risk of air embolus.

Brown and Fisk prefer pre-oxygenation and rapid sequence induction for injuries below the glottis. However, failed or misplaced intubation in this technique would necessitate positive pressure ventilation by facemask, with the risk of exacerbating any air leak. The tube itself can cause trauma in either this technique or inhalational induction, by enlarging the original injury.

The arguments for rapid sequence induction become stronger where there is a risk of pulmonary aspiration from a full stomach. In this case, anaesthesia was induced more than 8 hours after the last food was eaten, while the injury took place only 2 hours after that time. The injury might have caused gastric stasis and it was possible that the stomach was not empty at the time of surgery. In addition, inhalational induction would not be appropriate for a struggling child, who could be expected to build up considerable pressure in the airway, with disastrous results.

In the event, the overriding aim with this child was to prevent the need for positive pressure ventilation with or without a tracheal tube *in situ*. It was known that the child had an air leak and there was already a pneumomediastinum. Had cyclopropane been available, its judicious use for anaesthetic induction would have been considered. However, a small dose of thiopentone finally permitted tracheal intubation without the use of a muscle relaxant. The use of steroids was considered, with a view to preventing the development of oedema in the airway. There were, however, no signs of airway obstruction (such as stridor or voice change) and it was felt that the risk of sepsis outweighed the possible benefits of steroids in this case.

This case illustrates the need for individual assessment of patients with airway injury. Strict rules of management may not be helpful. In addition, by the time such a patient has arrived in the accident and emergency department, the

clinical situation may dictate rapid correction without referral to a paediatric surgical unit. There is a clear need for paediatric anaesthetic skills to be maintained in the context of a district general hospital.

References

1. HERRIN TJ, BRZUSTOWICZ R, HENDRICKSON M. Anaesthetic management of neck trauma. *Southern Medical Journal* 1979; **72**: 1102-6.
2. FELICIANO DV, BITONDO CG, MATTOX KL, ROMO T, BURCH JM, BEALL AC, JORDAN GL. Combined tracheoesophageal injuries. *American Journal of Surgery* 1985; **150**: 710-5.
3. GROVER FL, ELLESTAD C, AROM KV, ROOT HD, CRUZ AB, TRINKLE JK. Diagnosis and management of major tracheobronchial injuries. *Annals of Thoracic Surgery* 1979; **28**: 384-91.
4. BROWN TCK, FISK GC. *Anaesthesia for children*. Oxford: Blackwell, 1979: 317-8.

CASE REPORT

Epidural blockade in the treatment of preterm labour

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Summary

A case of premature labour induced by necrosis in a fibromyoma followed by laparotomy is described. Unsuccessful treatment with ritodrine was followed by successful treatment with epidural analgesia. The possible role of a sympathetic blockade is discussed.

Key words

Anaesthesia; obstetric.

Anaesthetic techniques, regional; epidural.

Intra-abdominal conditions that necessitate operation during pregnancy are often complicated by fetal death or premature labour.^{1–4} The most widely used treatment to prevent preterm delivery consists of bed rest, sedatives and possibly a β -sympathomimetic drug such as ritodrine.^{5,6} In some cases this treatment has been unsuccessful. Use of epidural blockade for the treatment of threatened preterm labour or abortion does not seem to have been reported previously.

Case history

A previously healthy 26-year-old woman who was in the 18th week of a twin pregnancy, was admitted to hospital with intermittent pain in the lower abdomen. Uterine contractions could be felt at intervals of 3–5 minutes. A tender swelling was present on the right side of the uterus. There was no dilatation of the cervix. Ultrasonography of the abdomen showed two live fetuses and a tumour that measured 8 × 8 cm located in the anterior wall of the uterus. The patient was treated with bed rest, diazepam and pethidine. The frequency and intensity of the contractions, as well as the pain, increased during the first 24 hours of admission and the treatment was therefore supplemented with intravenous ritodrine.

The contractions continued during the following 2 weeks despite the administration of ritodrine at dose levels up to 125 μ g/minute. Higher doses resulted in unacceptable tachycardia, with a pulse rate of more than 120 beats/minute and tremor. An attempt was made on several occasions to reduce the dosage of ritodrine but resulted in an increase in the intensity and frequency of the uterine contractions. Necrosis in a fibromyoma, leading to premature

contractions, was suspected as the size and tenderness of the tumour increased.

A laparotomy was carried out on the 15th day. Light general anaesthesia was supplemented with epidural analgesia with bupivacaine 0.5% via an epidural catheter inserted into the L_{2–3} interspace. The operation revealed a fibromyoma with a diameter of 8 cm, situated mainly within the uterine wall. Enucleation was therefore impossible.

Treatment with ritodrine 100 μ g/minute was continued for the following 48 hours and the epidural blockade was maintained by repeated injections of bupivacaine 0.5%, 10 ml every 2 hours; this led to a level of analgesia around L_{1–2}. The patient still complained of severe pain and the contractions were accompanied by effacement and dilatation of the cervix. Treatment with ritodrine was discontinued at this time and a continuous infusion of lignocaine 1.0% with adrenaline 5 μ g/ml, 20 ml/hour, commenced via the epidural catheter. This led to a level of analgesia around T_{8–9}. The contractions ceased within 12 hours of the start of this treatment but there were slight symptoms of intoxication in the form of shivering. As the patient was still in pain, the blockade was maintained for a further 3 days.

The remainder of the pregnancy was uncomplicated and she was delivered by Caesarean section in the 37th week of pregnancy.

Discussion

The rate of fetal loss after laparotomy during pregnancy is high. In a review of the literature covering the years 1963 to 1975, fetal or neonatal death was seen in around 35% of pregnant women subjected to operation for a perforated

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appendix with peritonitis, whereas it occurred in only 1.5% of women operated upon for uncomplicated appendicitis.² Other intra-abdominal conditions that require operation during pregnancy are uncommon and the frequency of fetal death or preterm labor cannot be estimated in the reported cases because the principles of treatment have varied. The most common treatment of threatened preterm delivery is bed rest and sedatives, possibly supplemented with a β -sympathomimetic agent such as ritodrine.^{5,6} Treatment with ritodrine has not been found to be more effective than placebo in the postponement of delivery in a number of investigations.⁵ The ability of β -sympathomimetic drugs to postpone delivery and improve the prognosis of the infant, however, cannot always be established.⁷

In the case reported here, threatened preterm delivery was induced by necrosis in a fibromyoma located intramurally, and by manipulation of the uterus during laparotomy. Treatment with bed rest, sedatives and ritodrine was unsuccessful and the patient suffered considerable pain. The contractions continued during epidural blockade that extended from segments L₁₋₂ and downwards, but extension of the block to T₈₋₉ by use of a continuous infusion resulted in cessation of the contractions within 12 hours. The remainder of the pregnancy was then uncomplicated.

Possible mechanisms responsible for the inhibitory effect of the epidural blockade upon the contractions, are inhibition of sympathetic reflex mechanisms and dilatation of blood vessels in partly ischaemic areas of the fibromyoma. The fact that the uterus receives its sympathetic innervation from segments T₆-T₁₂ and that the epidural blockade was effective only when its upper border reached segments T₈₋₉, favours the former explanation. The effect of the epidural blockade can thus be compared with its ability to restore gut motility to normal during the postoperative period.^{8,9} It has been shown that epidural blockade causes a decrease in resistance in the uterine side of the placental circulation,¹⁰ which favours the second explanation. The epidural block may have increased the blood flow in parts of the ischaemic fibromyoma, via the same mechanism, thereby withdrawing the stimulus to the contractions. We do not believe that inclusion of adrenaline in the local anaesthetic solution had any effect on uterine contractions, as ritodrine in a dose that produced a marked tachycardia, was already ineffective in inhibiting uterine contractions.

The good results obtained in the present case have led to the use of epidural blockade in three other pregnant women operated upon for suspected appendicitis. The operative findings were perforated appendix with peritonitis, appendicitis and a normal appendix. The course was uneventful in the woman with peritonitis. Slight uterine contractions were treated successfully by supplementary administration of ritodrine in the remaining two women. All the children were well and normally developed at follow-up one year later.

We therefore consider it possible that epidural blockade may impede or abolish contractions of the uterus after laparotomy in pregnant women. Further clinical trials are needed.

References

1. SAUNDERS P, MILTON PJD. Laparotomy during pregnancy: an assessment of diagnostic accuracy and fetal wastage. *British Medical Journal* 1973; **3**: 165-7.
2. BABAKNIA A, PARSA H, WOODRUFF JD. Appendicitis during pregnancy. *Obstetrics and Gynecology* 1977; **50**: 40-4.
3. HOROWITZ MD, GOMEZ GA, SANTIESTEBAN R, BURKETT G. Acute appendicitis during pregnancy. Diagnosis and management. *Archives of Surgery* 1985; **120**: 1362-7.
4. Appendicitis in pregnancy. EDITORIAL. *Lancet* 1986; **1**: 195-6.
5. LARSEN JF, HANSEN MK, HESSELDAL H, KRISTOFFERSEN K, LARSEN PK, OSLER M, WEBER J, ELTON K, LANGE A. Ritodrine in the treatment of preterm labour. A clinical trial to compare a standard treatment with three segments involving the use of ritodrine. *British Journal of Obstetrics and Gynaecology* 1980; **87**: 949-57.
6. MERKATZ IR, PETER JB, BARDEN TP. Ritodrine hydrochloride: a betamimetic agent for use in preterm labor. II. Evidence of efficacy. *Obstetrics and Gynecology* 1980; **56**: 7-12.
7. HEMMINKI E, STARFIELD B. Prevention and treatment of premature labour by drugs: review of controlled clinical trials. *British Journal of Obstetrics and Gynaecology* 1978; **85**: 411-7.
8. GELMAN S, FEIGENBERG Z, DINTZMAN M, LEVY E. Electroenterography after cholecystectomy. The role of high epidural analgesia. *Archives of Surgery* 1977; **112**: 580-3.
9. AHN H, LINDHAGEN J, BRONGE A, YGGE H. The effect of post-operative epidural local anaesthetics on gastrointestinal motility. In: *Abstracts, 5th Congress of the European Society of Regional Anaesthesia* 1986; **I**: 18A.
10. LAH F, GILES W, TRUDINGER B. Epidural anaesthesia and its effect on maternal and fetal placental arterial blood flow. In: BERGMANN H, KRAMAR H, STEINBEREITNER K, eds. *Abstracts, 7th European Congress of Anaesthesiology* 1986; **II**: 222-3.

CASE REPORT

Intrathecal buprenorphine for postoperative analgesia in the elderly patient

G. CAPOGNA, D. CELLENO, V. TAGARIELLO AND C. LOFFREDA-MANCINELLI

Summary

Ninety patients aged 56–85 years scheduled for suprapubic prostatectomy, randomly received intrathecally either bupivacaine 30 mg (group A, $n = 30$), bupivacaine 30 mg plus buprenorphine 0.03 mg (group B, $n = 30$) or bupivacaine 30 mg plus buprenorphine 0.045 mg (group C, $n = 30$). Prolonged postoperative analgesia, minimal disturbance of consciousness and comfortable breathing were common to the groups that received buprenorphine. The higher concentration of buprenorphine improved the quality and duration of analgesia. The only side effects found in the buprenorphine groups were nausea and vomiting in 11 and 14 patients, respectively, in groups B and C. Our study shows that buprenorphine is an effective analgesic, suitable for the management of postoperative pain in elderly patients.

Key words

Pain; postoperative.

Anaesthetic techniques, regional; spinal.

Analgesics, narcotic; buprenorphine.

Opioids are commonly used to treat postoperative pain, and intrathecal morphine is a routine method that provides prolonged postoperative analgesia.^{1–3} Side effects such as itching, nausea, vomiting and possible respiratory depression have been reported in a number of cases.^{4,5} Predisposing factors for the latter appear to be advanced age,^{2,6,7} use of water-soluble opioids,⁴ intra-operative artificial ventilation² and concomitant administration of other central nervous system depressant drugs.² Age may be a major risk factor for respiratory depression by its influence on spinal fluid volume and pressure.^{5,8,9}

Epidural buprenorphine has been reported to provide good postoperative analgesia while it reduces many of the side effects commonly seen with morphine.^{10–13} The high lipophilicity of buprenorphine allows rapid systemic absorption from the epidural site.¹⁴ The low dural permeability suggests that buprenorphine would be a poor choice as an extradural narcotic.¹⁴ Its high lipophilicity and high molecular weight (481) may be useful to prevent rostral spread and common side effects once the drug is given intrathecally. Buprenorphine can be administered safely in the subarachnoid space.^{15,16} The intrathecal route has the advantage of greater technical ease than the epidural technique, and a single injection produces pain relief of sufficient duration for most

postoperative patients.¹⁷ This double-blind study was performed to determine the effects of two doses of intrathecal buprenorphine for postoperative pain relief in elderly patients.

Methods

Ninety men aged 56–85 years (Table 1) scheduled for suprapubic prostatectomy were randomly assigned to one of three groups: group A, hyperbaric bupivacaine 30 mg ($n = 30$); group B, hyperbaric bupivacaine 30 mg plus buprenorphine 0.03 mg ($n = 30$); and group C, hyperbaric bupivacaine 30 mg plus buprenorphine 0.045 mg ($n = 30$). The patients were blind to the drug given. Informed consent was obtained from each patient and the study was approved by the Human Investigation Committee.

An intravenous infusion of 500–1000 ml Ringer's lactate solution was given 30 minutes before the start of surgery. The block was performed with a standard technique using a 25-gauge needle at the L₂–L₃ or L₃–L₄ interspace. The appropriate dose of buprenorphine was added to 3 ml 1% hyperbaric bupivacaine. Heart rate, arterial blood pressure and respiratory rate were monitored every 2 hours post-operatively. Arterial blood gas samples and analgesia by

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the visual analogue score¹⁸ were evaluated every 2 hours for the first 8 hours and at 12 and 24 hours by an independent observer.

The incidence of nausea, vomiting, pruritus and sedation was recorded. The patient was no longer assessed for analgesia when the initial spinal dose wore off, and supplementation was provided with buprenorphine 0.2 mg intramuscularly. All patients were maintained in a 15° head-up position during surgery and in the recovery room.

Comparison among the three groups was done using the Kruskal-Wallis test and Chi-square test and between any two groups using the Mann-Whitney Wilcoxon test. Significant differences were accepted at $p < 0.05$. No alpha adjustment was made because of multiple comparison.

Results

The difference in pain-free interval among the groups was significant ($p < 0.05$). The mean pain-free interval was 103.45 minutes in the control group. Buprenorphine 0.045 mg was associated with longer postoperative analgesia compared with 0.03 mg ($p < 0.05$, Table 1). In group B, however, pain increased gradually from 5 to 8 hours, and in group C pain increased from 7 to 12 hours (Fig. 1).

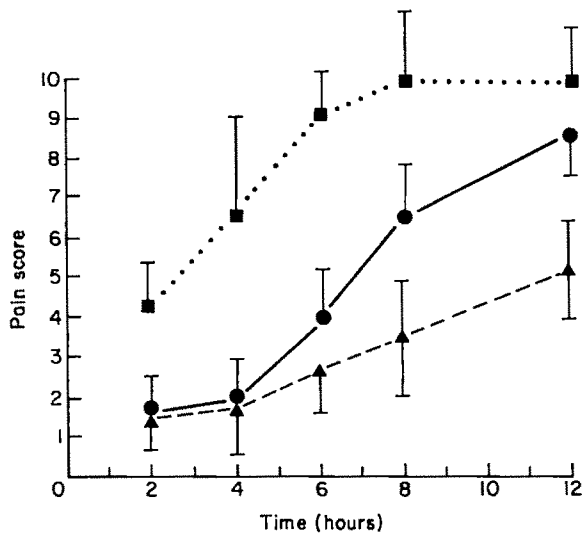


Fig. 1. Visual analogue pain score. ···, Group A; —, group B; ---, group C.

The mean respiratory rate in all three groups during the first 12 hours after surgery did not differ significantly and remained within the physiological range (Fig. 2); it transiently decreased below 10 breaths/minute in one patient in group C but required no treatment. No further problems were encountered postoperatively. Heart rate and arterial blood pressure remained within the physiological range during the observation time and there were no significant

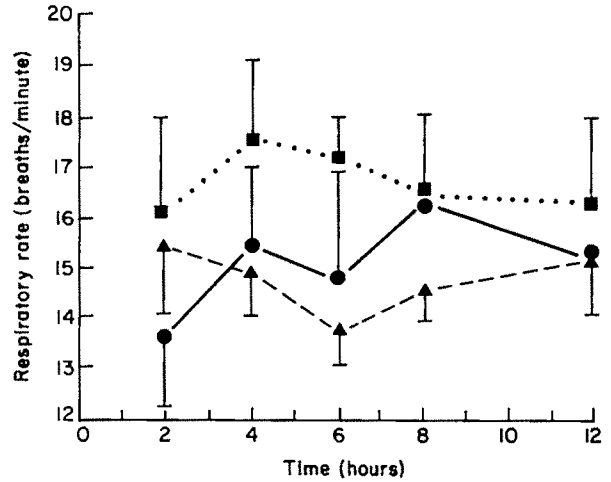


Fig. 2. Respiratory rate. ···, Group A; —, group B; ---, group C.

differences in either base excess or mean oxygen tension and oxygen saturation among the groups. Mean values of carbon dioxide tension were not significantly different among the three groups (Fig. 3).

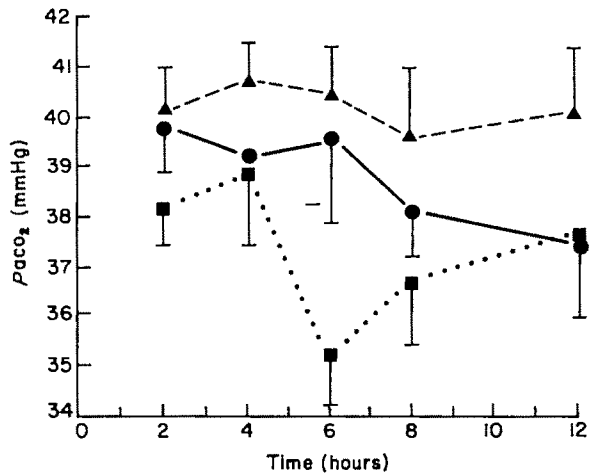


Fig. 3. Arterial carbon dioxide tension. ···, Group A; —, group B; ---, group C.

Nausea and vomiting occurred in 11 patients who received 0.03 mg buprenorphine and in 14 patients who received the larger dose. This was significantly more common than in those who did not receive the drug ($p < 0.05$, Table 2).

Discussion

Numerous studies since the first clinical use of intrathecal morphine in 1979, have confirmed the efficacy of spinally administered opioids for postoperative pain

Table 1. Patient data. Values expressed as mean (SD).

	Group A	Group B	Group C
Age, years	65.2 (6.3)	64.3 (5.9)	63.6 (5.1)
Weight, kg	76.6 (9.4)	73.5 (8.1)	72.6 (10.8)
Duration of surgery, minutes	119 (12)	105 (11)	95 (14)
Pain-free interval, minutes	103.45* (9)	183.06† (31)	430.16 (24)

* $p < 0.01$ compared with groups B and C.

† $p < 0.05$ compared with group C.

Table 2. Non-respiratory side effects.

	Group A	Group B	Group C
Nausea	2 (6.6%)	8 (26.6%)*	9 (29.9%)*
Vomiting	1 (3.3%)	3 (10%)*	5 (16.6%)*
Pruritus	0	1 (3.3%)	2 (6.6%)
Sedation	1 (3.3%)	2 (6.6%)	1 (3.3%)
Headache	1 (3.3%)	0	1 (3.3%)

* p < 0.05 compared with group A.

relief.^{1-3,15-17,19} However, opioids do not remain localised to the site of epidural and/or intrathecal injection. After spinal administration opioids undergo redistribution by rostral spread, which explains the occurrence of nausea and vomiting in 15-35% of patients, respiratory depression and the spread of hypo-algesia.^{19,20}

An understanding of cerebrospinal fluid dynamics and the pharmacokinetics of intrathecal opioids is essential to explain such effects. Opioids reach the cisterns of the brain 3-6 hours after intrathecal administration and then the respiratory centres through the ventral pons.^{20,21} A lipid soluble nonionised drug like buprenorphine passes rapidly via the arachnoid granulations into venous and lymphatic vessels, which allows a minimal increase of cerebrospinal fluid concentration with a minor risk of respiratory depression.¹ The effect of other lipophilic opiates is brief because of their rapid clearance from spinal cord sites. In addition, buprenorphine, because of its high affinity for opiate receptors,¹⁴ is likely to produce a greater duration of analgesia than reported for other lipophilic agents.^{19,22,23} Use of the sitting position, hyperbaric solutions,²⁰ lower doses of systemic analgesics⁷ and lipid soluble opioids²⁴ are all means to decrease the incidence of respiratory depression.

Elderly patients have greater risks of infective, thromboembolic and respiratory postoperative complications. Furthermore, they are more sensitive to the consciousness depressant effects of commonly used doses of parenteral narcotics. In the present study, intrathecal buprenorphine provided postoperative analgesia with minimal disturbance of consciousness. Comfortable breathing reduced the risks of postoperative complications. Intrathecal administration of buprenorphine 0.03 mg or 0.045 mg may be used for postoperative analgesia in elderly patients. The higher concentration offers more prolonged analgesia without any further significant increase in side effects.

References

1. FOOLEY KM, INTURRISI CE. *Opioid analgesics in the management of clinical pain*. New York: Raven Press, 1986.
2. GJESSING T, TOMLIN PJ. Postoperative pain control with intrathecal morphine. *Anaesthesia* 1981; **36**: 268-76.
3. WANG JK, NAUSS LA, THOMAS JE. Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979; **50**: 149-51.
4. GUSTAFSSON LL, SHILDT B, JACOBSEN K. Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. *British Journal of Anaesthesia* 1982; **54**: 479-86.
5. BOAS RA. Hazards of epidural morphine. *Anesthesia and Intensive Care* 1980; **8**: 377-8.
6. KLINCK JR, LINDOP MJ. Epidural morphine in the elderly: a controlled trial after upper abdominal surgery. *Anaesthesia* 1982; **37**: 907.
7. GUSTAFSSON LL, FEYCHTING B, KLINGSTEDT C. Late respiratory depression after concomitant use of morphine epidurally and parenterally. *Lancet* 1981; **1**: 892-3.
8. CHRISTENSEN V. Respiratory depression after extradural morphine. *British Journal of Anaesthesia* 1980; **52**: 841.
9. CRAWFORD RD, BATRA MS, FOX F. Epidural morphine dose response for postoperative analgesia. *Anesthesiology* 1981; **55**: A150.
10. ROMDOMANSKA M, DE CASTRO J, LECRON L. The use of epidural buprenorphine for the treatment of postoperative pain. In: YAKSH TL, MULLER H, eds. *Spinal opiate analgesia*. Berlin: Springer, 1982: 91-4.
11. LANZ E, SIMKO G, THEISS D, GLOCKE MH. Epidural buprenorphine—a double-blind study of postoperative analgesia and side effects. *Anesthesia and Analgesia* 1984; **63**: 593-8.
12. GUNDERSEN RY, ANDERSEN R, NARVERUD G. Postoperative pain relief with high-dose epidural buprenorphine: a double-blind study. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 664-7.
13. SRIVASTAVA S. Epidural buprenorphine for postoperative pain relief. *Anaesthesia* 1982; **37**: 699.
14. MOORE RA, BULLINGHAM RES, MCQUAY HJ, HAND CW, ASPEL JB, ALLEN MC, THOMAS D. Dural permeability to narcotics: *in vitro* determination and application to extradural administration. *British Journal of Anaesthesia* 1982; **54**: 1117-28.
15. BORNER U, MULLER H, STONAYOU M, HEMPELMANN G. Epidural opiate analgesia. Gewebe- und liquorwertraglichkeit der opiate. *Anaesthesist* 1980; **29**: 570-1.
16. COUSINS JM, BRINDENBAUGH PO. Spinal opioids and pain relief in acute care. In: COUSINS MJ, PHILLIPS GD, eds. *Acute pain management*. New York: Churchill-Livingstone, 1986: 156-7.
17. SAMI K, CHAUVIN M, VIARS P. Postoperative spinal analgesia with morphine. *British Journal of Anaesthesia* 1981; **53**: 817.
18. SCOTT J, HUSKISSON EC. Graphic representation of pain. *Pain* 1976; **2**: 175-84.
19. YAKSH TL. Spinal opiate analgesia: characteristics and principles of action. *Pain* 1981; **11**: 293-346.
20. COUSINS MJ, MATHER LE. Intrathecal and epidural administration of opioids. *Anesthesiology* 1984; **61**: 276-310.
21. DI CHIRO G. Movement of the cerebrospinal fluid in human beings. *Nature* 1964; **204**: 290.
22. TUNG AS, YAKSH TL. The antinociceptive effects of epidural opiates in the cat: studies on the pharmacology and the effects of lipophilicity in spinal analgesia. *Pain* 1982; **12**: 343-56.
23. HAMBROOK JM, RANCE MJ. The interaction of buprenorphine with opiate receptor. In: KOSTERLITZ H, ed. *Opiate and endogenous opioid peptides*. Amsterdam: Elsevier-North-Holland Biomedical, 1976: 295-301.
24. LAM AM, KNILL RL, THOMPSON WR, CLEMENT JL, VARKEY GP, SPOEREL WE. Epidural fentanyl does not cause delayed respiratory depression. *Canadian Anaesthetists' Society Journal* 1983; **30**: S78.

APPARATUS

A comparison of oxygen therapy devices used in the postoperative recovery period

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Summary

Seventy-one patients scheduled to undergo upper or lower abdominal surgical procedures were allocated at random to one of seven treatment groups: in the recovery room they were to receive oxygen via a 40% Ventimask with 10 litres/minute oxygen flow, or via either a Hudson mask or a nasal cannula with 3, 6 or 9 litres/minute oxygen flow. The 40% Ventimask gave the most consistent, satisfactory postoperative values of PaO_2 but the much cheaper nasal cannula at 6 or 9 litres/minute was generally adequate in conscious patients. The performance of the intermediately priced Hudson mask was similar to that of the nasal cannula at these flows. The unconscious state was associated with a 45% lower PaO_2 than the rousable or awake states. Differences between the treatments with regard to postoperative PaCO_2 were small and non-significant. The nasal cannula with 6 litres/minute humidified oxygen flow is recommended for routine treatment, and the Ventimask for unconscious patients.

Key words

Apparatus; Ventimask, facemask, nasal cannula.
Oxygen therapy; postoperative.

There is ample evidence for the existence of postoperative arterial hypoxaemia and that it may result in increased morbidity and mortality.^{1,2} There are many devices for administering oxygen. Leigh^{3,4} has classified them into fixed performance and variable performance devices.

The fixed performance type are patient-independent and deliver oxygen and entrained air at flows above the peak inspiratory flow rate of the recipient, thus preventing re-breathing and resulting in an inspired oxygen concentration which is fixed and predictable. These masks require a high oxygen flow rate for a given FiO_2 , which makes them both noisy and expensive to run.⁵ An example of this type of device is the Vickers Ventimask.

The variable performance devices are patient-dependent and were divided into two groups by Leigh:⁴ those which result in re-breathing (e.g. M.C. (Mary Catterall) mask, Edinburgh mask, Hudson low-concentration mask) and those which do not (nasal cannulae and nasal catheters). The masks all consist of a vented enclosure, applied over the nose and mouth. The oxygen is supplied into this enclosure with little or no entrainment, so that the deadspace of the respiratory system is likely to be increased. The nasal

cannula is inserted into one nostril with a foam seal so that the oxygen supplied to it is delivered to the nasopharynx which acts as a reservoir; the inhaled oxygen concentration is thereby increased. The cannula imposes no apparatus deadspace and it seems likely that the oxygen flow may even erode the physiological deadspace, particularly at high flows.

The variable performance mask is the device most commonly used in postoperative oxygen therapy. We wished to know whether the advantages of a fixed performance mask were sufficient in these circumstances to justify the greater cost (about twice that of a variable performance mask) and, on the other hand, whether a nasal cannula (at about half the cost of a variable performance mask) would perform just as well.

Different types of mask (but not nasal cannulae) have been compared in a laboratory model⁶ and studies have been undertaken in patients to assess, separately, the effectiveness of fixed performance masks,^{7,8} variable performance masks⁹ and nasal cannulae.^{10–12} The only comparative clinical study which we have traced¹³ was performed on essentially healthy volunteers and relied

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on measurements of gas concentrations. Therefore we undertook a study in postoperative patients and measured blood gas tensions. We chose to compare, after abdominal surgery, the 40% Vickers Ventimask (with the recommended oxygen flow of 10 litres/minute), the Hudson mask (elongated 'see-Thru', Cat. No. 1049, Henleys Medical Supplies Ltd) with flows of 3, 6 and 9 litres/minute, and the nasal cannula (Unoplast nasal oxygen cannula, Code No. 200-12-040) also with flows of 3, 6 and 9 litres/minute.

Method

The study was approved by the ethics committees of the University Hospital of Wales, Cardiff, and the Royal Gwent Hospital, Newport. The selection of patients was intended to provide a representative sample of those commonly treated in this way postoperatively: over 18 years of age, undergoing major elective upper and lower abdominal surgery, including gynaecological surgery, ASA grades 1-3. A total of 71 patients consented to participate.

Arterial blood gas analysis was carried out pre-operatively on each patient. Various anaesthetists were involved but their choice of anaesthetic technique was constrained as follows: thiopentone, muscle relaxant, narcotic, nitrous oxide and volatile agent, with intermittent positive pressure ventilation of the lungs, followed by reversal of the relaxant by neostigmine with atropine. After surgery, the patients were transferred to the recovery ward where they were allocated at random to one of the seven groups shown in Table 1. Arterial blood gas analysis was repeated 20 minutes after admission to the recovery room.

Table 1. The seven treatment groups.

Group	Mask	Oxygen flow (litres/minute)
1	40% Vickers Ventimask	10
2	Hudson mask	3
3	Hudson mask	6
4	Hudson mask	9
5	Nasal cannula *	3
6	Nasal cannula *	6
7	Nasal cannula *	9

* The nasal cannula was inserted 2-3 cm into one nostril and its oxygen supply was humidified.

Postoperative P_{aO_2} and P_{aCO_2} are likely to be influenced by several circumstances in addition to the choice of mask and oxygen flow rate. Therefore all the variables listed in Table 2 were recorded, by one observer (A.B.W.); most of the information was obtained from the anaesthetic chart. The results were analysed by means of a multiple regression modelling technique (see Appendix). The objective of such modelling is to identify and quantify as many as possible of the systematic effects of the independent variables on the dependent variable (primarily the postoperative P_{aO_2}), thereby leaving as little variation as possible to be ascribed to random error. This reduces the residual variance (the scatter of individual observed values of P_{aO_2} about the values estimated from the systematic elements of the model) and thereby increases the precision of estimates of all means and coefficients. It also reduces any bias which may otherwise arise from chance differences between treatment groups. For example, a difference in mean age between two groups, if coupled with an appreciable dependence of P_{aO_2} on age, will contribute to the difference in P_{aO_2} between

Table 2. Observations recorded, with means and ranges of values, or numbers of cases in each category.

	Mean	Range
<i>Pre-operative</i>		
Age, years	55.6	22-86
pH	7.41	7.36-7.46
P_{aCO_2} , kPa	4.85	3.9-6.0
P_{aO_2} , kPa	12.2	8.1-16.6
<i>Peroperative</i>		
Site of operation		
Upper abdomen		28 patients
Lower abdomen		43 patients
Volume of crystalloid solution administered, ml	741	0-2800
Volume of colloid solution administered, ml	233	0-1500
Duration of operation, minutes	98.4	35-215
<i>Twenty minutes postoperative</i>		
Level of consciousness		
Unconscious		4 patients
Rousable		28 patients
Awake		39 patients
State of airway		
Stridor		1 patient
Noisy breathing		4 patients
Normal		66 patients
P_{aO_2} , kPa	19.3 *	7.1-49.7
P_{aCO_2} , kPa	5.7	4.3-9.5

* Geometric mean.

the groups and distort any difference that results from the different treatments. The model assumed (see Appendix) that any independent variable which significantly affected the postoperative P_{aO_2} or P_{aCO_2} did so in the same way for all combinations of mask and oxygen flow.

Results

None of the 71 patients was withdrawn from the study. There were 10 patients in each group except for the group who received 9 litres/minute oxygen via the Hudson mask, which had 11 patients. The means and ranges of all variables are shown in Table 2.

It was decided in modelling the results for postoperative P_{aO_2} (see Appendix), to handle the different combinations of mask and oxygen flow as seven different treatments. Of the 10 additional variables which might have been expected to influence the postoperative P_{aO_2} (Table 2), only age, volume of crystalloid solution, and level of consciousness were found to be significant. Relevant group means and numbers of patients are listed in Table 3. Equation (2) in the Appendix predicts that each decade increase in age results in a 5% decrease in P_{aO_2} (95% confidence interval 1.4-8.7%); that each 100-ml extra volume of crystalloid solution administered during the operation is associated with another 3.8% lower postoperative P_{aO_2} (95% interval 3.0-4.6%); and that the unconscious state is associated with a 45% lower P_{aO_2} than the rousable or awake states (95% interval 21-61% lower).

Figure 1 shows postoperative P_{aO_2} plotted against oxygen flow in terms of the mean value predicted by the model for each of the seven treatments, for a patient aged 60 who has received 1000 ml of crystalloid solution and is rousable or awake. The error bars indicate, for each treatment, the 95% confidence interval for a single new

Table 3. Group means and numbers of patients relevant to the modelling of postoperative P_{aO_2} .

	Mean age, years	Mean volume of crystalloid solution, ml	Number of patients			Geometric mean postoperative P_{aO_2} , kPa
			Unconscious	Rousable	Awake	
Ventimask	54.0	750	0	3	7	20.6
Hudson mask						
3 litres/minute	54.4	680	1	2	7	18.6
6 litres/minute	56.9	710	0	1	9	20.5
9 litres/minute	52.3	1036	0	6	5	21.5
Nasal cannula						
3 litres/minute	62.0	650	0	8	2	12.1
6 litres/minute	53.2	730	2	3	5	21.0
9 litres/minute	56.4	600	1	5	4	23.6

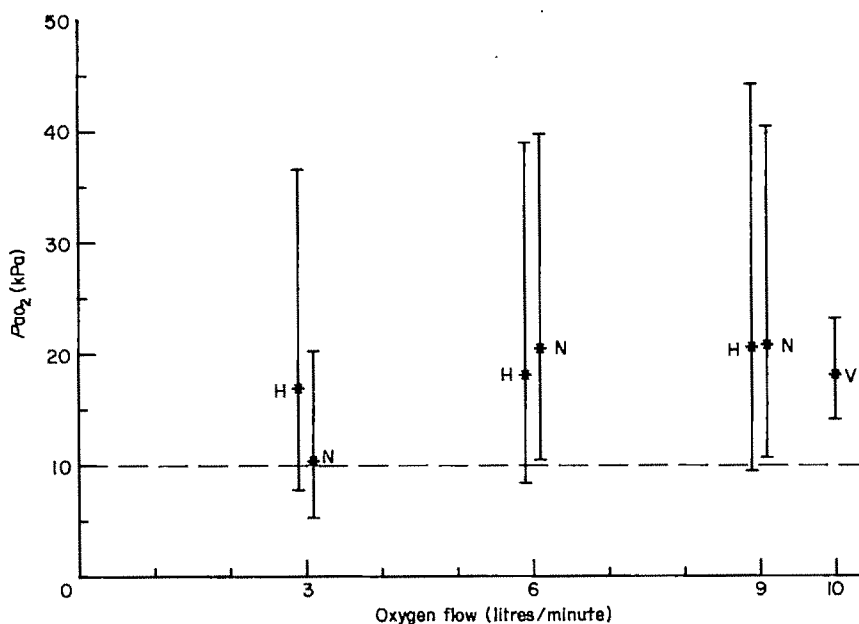


Fig. 1. Predicted means (*) and 95% confidence limits for individual future patients, of postoperative P_{aO_2} for the Ventimask (V), Hudson mask (H) and nasal cannula (N). The predictions are for a patient aged 60 years, who has received 1 litre of crystalloid solution peroperatively and is rousable or awake. The horizontal line at 10 kPa indicates a likely 'target minimum' P_{aO_2} .

observation, i.e. the range of values of P_{aO_2} likely to be encountered in 95% of patients with these characteristics. It follows that 2.5% of patients are likely to have values of P_{aO_2} below the range and 2.5% to have values above. (The asymmetry of the limits of the range arises because the analysis was performed in terms of $\log P_{aO_2}$: see Appendix.)

The only significant difference between treatments in terms of predicted mean values of P_{aO_2} , was that the nasal cannula with 3 litres/minute oxygen flow gave lower values of P_{aO_2} ($t = 4.9$, d.f. = 60, $p < 0.0001$ in comparison with the Ventimask; $t = 3.0$, d.f. = 60, $p = 0.004$ in comparison with the Hudson mask at 3 litres/minute). However, the variability of the results with the Hudson mask and nasal cannula was much greater than with the Ventimask. Thus, the predicted mean P_{aO_2} values for 6 or 9 litres/minute flow through the Hudson mask or nasal cannula were as good as, or better than those for the Ventimask with 10 litres/minute but the confidence interval for future results was very much wider than that for the Ventimask.

The data were grouped according to mask in modelling the

Table 4. Group means relevant to the modelling of postoperative P_{aCO_2} .

	Mean pre-operative P_{aCO_2} , kPa	Mean duration of anaesthesia, minutes	Mean postoperative P_{aCO_2} , kPa
Ventimask	4.97	89	5.84
Hudson mask	4.83	102	5.75
Nasal cannula	4.86	97	5.56

results for postoperative P_{aCO_2} (see Appendix). Relevant group means are given in Table 4. Significant additional explanatory variables were pre-operative P_{aCO_2} and duration of operation. Equation (3) in the Appendix indicates that postoperative P_{aCO_2} increased at the rate of 0.78 kPa (95% confidence interval 0.56–1.00 kPa) per kPa increase in pre-operative P_{aCO_2} , and decreased at the rate of 0.23 kPa (0.03–0.42 kPa) per hour increase in duration of operation. Also, for any given pre-operative P_{aCO_2} and for any given duration of anaesthesia, the predicted value of postoperative P_{aCO_2} for the Hudson mask was greater than

for the Ventimask, but only by 0.06 kPa (95% interval 0.31 kPa less to 0.44 kPa greater). The predicted value for the nasal cannula was less than for the Ventimask, but only by 0.16 kPa (0.40 kPa less to 0.08 kPa greater). The P_{aCO_2} for the nasal cannula decreased by 0.02 kPa for each 1 litre/minute increase in oxygen flow (decreased by 0.09 to increased by 0.05 kPa).

Discussion

It is reasonable to aim for a P_{aO_2} of at least 10 kPa (corresponding to 95% saturation with a normal oxygen dissociation curve) if the objective of postoperative oxygen therapy is taken to be the maintenance of near maximum saturation of arterial blood. Figure 1 indicates that very few patients would be expected to fall short of this aim with the Ventimask, fewer than 2.5% with the nasal cannula with 6 or 9 litres/minute oxygen flow, and only slightly more than 2.5% with the Hudson mask with these flows. However, nearly 50% of patients would fall short with the nasal cannula with only 3 litres/minute oxygen flow. It should be remembered that these results are for a patient aged 60 years, who has received 1000 ml of crystalloid solution and who is in the rousable or awake state. Therefore, all the treatments will be less satisfactory for patients who are much older than 60 years, who receive larger volumes of crystalloid solution, and especially those who are unconscious.

The effects of age and level of consciousness on postoperative P_{aO_2} are at least qualitatively plausible and the 'effect' of crystalloid solution can be explained by postulating that the volume administered provides a rough measure of the degree of trauma of the operation. On that basis it might be expected that the volume of colloid solution would also be significant, but it was not. There are two possible explanations. First, in some patients, 500 ml was administered as a matter of prophylactic policy rather than on the basis of currently assessed need; secondly, the volumes of colloid solution administered to different patients were zero or closely clustered around 500, 1000 or 1500 ml, whereas the volumes of crystalloid solution were more continuously distributed from zero to 1500 ml with one patient who received 2800 ml. The fit of the model to the data was poorer when total fluid volume was substituted for volume of crystalloid solution in the model.

The differences in P_{aO_2} between the types of mask and cannula were in the directions to be expected from the differences of added (or eroded) deadspace, mentioned in the introduction, but not significantly different from zero. The smallness of the differences may be partly due to the patient compensating by changes of total ventilation. If so, this may constitute an additional reason for preferring the nasal cannula.

Thus the 40% Ventimask, with 10 litres/minute oxygen flow, gave the most consistent, satisfactory results, but the nasal cannula, at about a quarter of the price, with a flow of only 6 litres/minute, was adequate for the great majority of patients. The Ventimask seems to be indicated in the patient who is still unconscious, and it may also be beneficial in patients who are elderly or have received large volumes of crystalloid solution, or show other evidence of more than average surgical trauma. The differences of P_{aCO_2} between types of mask and cannula do not conflict with these conclusions.

Acknowledgments

We are grateful to Dr T.J. Peters of the Department of Medical Computing and Statistics for statistical guidance, particularly for reassurance on the validity of the iteratively weighted regression technique and for advice on the calculation of 95% confidence intervals for future results. We are also grateful to the staff of the Biochemistry Laboratories, and to the nursing staff of the recovery rooms, in the University Hospital of Wales, Cardiff, and the Royal Gwent Hospital, Newport for their cooperation.

Appendix

The main independent variables in the model are the ones that were deliberately varied as part of the experimental protocol, i.e. the treatments. These could be regarded either as one of three masks combined with one of four possible oxygen flows (but not all flows with all masks), or simply as seven different mask-flow combinations.

Additional independent variables can be any which satisfy all the following criteria:

- values of the variable recorded in all patients;
- the variable can be expected, *a priori*, to influence the dependent variable and not to be influenced by it;
- the variable does, in fact, influence the dependent variable in the expected direction and significantly improves the quality of fit of the model.

The first two criteria led to the variables (other than postoperative P_{aO_2} and P_{aCO_2}) listed in Table 2. (Although very low values of P_{aO_2} can lead to unconsciousness, it was considered that the values observed in this study were not low enough for this to apply, but that the level of consciousness could indeed influence P_{aO_2} .)

In modelling the postoperative P_{aO_2} results, mask and oxygen flow were initially handled as separate, independent treatment variables, in the hope of estimating a continuous variation of P_{aO_2} with oxygen flow and hence determining 'equipotent flows' for the three masks by an extension of the method described by Mapleson¹⁴ and by Thomas and others.¹⁵ However, this revealed that, with the Hudson mask, P_{aO_2} was not significantly dependent on oxygen flow and that, with the nasal cannula, there was a strong suggestion of a non-linear relationship between P_{aO_2} and flow (see Fig. 1). Therefore, the seven mask-flow combinations were handled as seven separate treatments.

The modelling was done with the statistical package GLIM (Generalised Linear Interactive Modelling)¹⁶ although only the basic, multiple linear regression facilities were used. The model can be represented by the equation

$$y = b_0 + b_1x_1 + b_2x_2 + \dots + c_1 + c_2 + \dots \quad (1)$$

where the x s are the continuous independent variables, such as pH and age, the b s are the estimates of the expected rates of change of y with the corresponding x s, and the c s are the estimates of the coefficients for the independent variables with discrete levels: one c for each such variable but a different value of that c for each such variable but a different value of that c for each level of the variable (two for the two different sites of operation, three for the levels of consciousness, three for the states of airway and seven for the seven treatments).

As might be expected from the shape of the oxygen dissociation curve, the distribution of the values of P_{aO_2} was positively skew. However, the distribution of the residuals of the model was rendered symmetrical and approximately normal by working with $y = \log(P_{aO_2})$. Initially, all possible additional independent variables

were included. Then those which yielded the smallest t values (estimate of coefficient divided by the standard error of that estimate) were eliminated a few at a time until only variables with significant coefficients ($t > 2$) remained. (Discrete variables were retained if their omission significantly worsened the fit according to an F test.) This left age, volume of crystalloid solution, level of consciousness, and treatment as significant predictors of P_{aO_2} . Interactions between these predictors (e.g. P_{aO_2} varying with age at a different rate with different treatments) were excluded from the model because none of them was significant. Thus the model assumed that each significant additional variable had the same effect with all treatments.

On plotting the residuals of this model against the fitted values, separately for each mask, it was evident that, although they were reasonably normally distributed with a variance that did not change noticeably with fitted value, the variance was considerably greater for the Hudson mask and nasal cannula than for the Ventimask. Therefore the model was refitted with the individual observations for each mask weighted in inverse proportion to the variance of the residuals for that mask in the previous model. This process was iterated until there was little further change in residuals or coefficients, so that the weighting was very nearly in inverse proportion to the variances of the residuals in the *current* model. This yielded the equation:

$$y = 1.290 - 0.00209x_1 - 0.000164x_2 + c_1 + c_2 \quad (2)$$

where

- $y = \log (P_{aO_2}, \text{kPa})$
- $x_1 = \text{age, years}$
- $x_2 = \text{volume of crystalloid solution, ml}$
- $c_1 = 0$ for consciousness level 1
0.271 for level 2
0.255 for level 3
- $c_2 = 0$ for Ventimask
-0.029 for Hudson mask with 3 litres/minute oxygen
0.000 for Hudson with 6 litres/minute oxygen
0.056 for Hudson with 9 litres/minute oxygen
-0.239 for nasal cannula with 3 litres/minute oxygen
0.054 for nasal cannula with 6 litres/minute oxygen
0.061 for nasal cannula with 9 litres/minute oxygen

The plausibility of the dependence on these additional independent variables is argued in the main text.

No transformation was necessary in modelling the post-operative P_{aCO_2} results but it was found that flow had only a very small, non-significant effect. Therefore the results were grouped according to mask. The only significant additional variables were pre-operative P_{aCO_2} and duration of operation. Again, there were no significant interactions. Flow was retained as an additional variable, in order to determine the confidence limits of its effect with the nasal cannula. Iterative weighting was again necessary and led to the equation:

$$y = 2.29 + 0.782x_1 - 0.227x_2 + c_1 + c_2x_3 \quad (3)$$

where

- $y = \text{postoperative } P_{aCO_2}, \text{ kPa}$
- $x_1 = \text{pre-operative } P_{aCO_2}, \text{ pKa}$
- $x_2 = \text{duration of operation, hours}$
- $x_3 = \text{difference of oxygen flow from mean flow for mask (litres/minute)}$
- $c_1 = 0$ kPa for Ventimask
0.064 kPa for Hudson mask
-0.161 kPa for nasal cannula
- $c_2 = 0.020$ kPa/litre/minute for the Hudson mask
-0.018 kPa/litre/minute for the nasal cannula

(The value of c_2 for the Ventimask is indeterminate because only one flow was used.)

References

- MARSHALL BE, WYCHE MQ. Hypoxemia during and after anesthesia. *Anesthesiology* 1972; **37**: 178-209.
- LEIGH JM. Postoperative oxygen administration. *British Journal of Anaesthesia* 1975; **47**: 108-12.
- LEIGH JM. Variation in performance of oxygen therapy devices. *Anaesthesia* 1970; **25**: 210-22.
- LEIGH JM. Variation in the performance of oxygen therapy devices. Hunterian Lecture delivered on 11 October 1972. *Annals of the Royal College of Surgeons of England* 1973; **52**: 234-53.
- LEIGH JM. Audible noise levels of oxygen masks operating on venturi principle. *British Medical Journal* 1973; **4**: 652.
- BETHUNE DW, COLLIS JM. The evaluation of oxygen masks. A mechanical method. *Anaesthesia* 1967; **22**: 43-54.
- DRUMMOND GB. Postoperative hypoxaemia and oxygen therapy. *British Journal of Anaesthesia* 1975; **47**: 491-9.
- DRUMMOND GB, WRIGHT DJ. Oxygen therapy after abdominal surgery. *British Journal of Anaesthesia* 1977; **49**: 789-97.
- CONWAY CM, PAYNE JP. Post-operative hypoxaemia and oxygen therapy. *British Medical Journal* 1963; **1**: 844-5.
- JACOBSEN JB, NIELSEN H, BRINKLOV MM, STOKKE DB, HARTMANN-ANDERSEN JF. Efficiency of two variable performance techniques of oxygen therapy in relieving post-operative hypoxaemia. *British Journal of Anaesthesia* 1980; **52**: 925-30.
- TANTUM KR. Comparison of nasal catheter and nasal cannula in patients recovering from general anesthesia. *Anesthesiology* 1969; **31**: 376-7.
- HELLER ML, WATSON TR, IMREDDY DS. Postoperative hypoxemia and its treatment with nasal oxygen: polarographic study. *Surgery* 1965; **58**: 819-23.
- KORY RC, BERGMANN JC, SWEET RD, SMITH JR. Comparative evaluation of oxygen therapy techniques. *Journal of the American Medical Association* 1962; **179**: 767-72.
- MAPLESON WW. The use of GLIM and the bootstrap in assessing a clinical trial of two drugs. *Statistics in Medicine* 1986; **5**: 363-74.
- THOMAS DL, VAUGHAN RS, VICKERS MD, MAPLESON WW. A comparison of temazepam elixir and trimeprazine syrup as oral premedication in children undergoing tonsillectomy and associated procedures. *British Journal of Anaesthesia* 1987; **59**: 424-30.
- BAKER DJ, NELDER JA. *The GLIM system, release 3*. Oxford: Numerical Algorithms Group, 1978.

APPARATUS

A comparison of two pulse oximeters

Assessment of accuracy at low arterial saturation in paediatric surgical patients

S. A. RIDLEY

Summary

The accuracy of the Ohmeda Biox 3700 and the Nellcor N100E was assessed in 25 cyanosed children. The readings obtained from the two pulse oximeters were compared with arterial blood measurements using a Radiometer OSM-2 co-oximeter. Both pulse oximeters differed significantly from the co-oximeter measurements and in these patients the error of both machines exceeded the manufacturers' claims. However, the machines appeared to reflect changes in saturation accurately in the same patient.

Key words

Measurement techniques; pulse oximetry.
Oxygen; arterial saturation.

Pulse oximetry is used increasingly to provide a continuous monitor of arterial oxygen saturation (Sao_2) in anaesthetic practice and the intensive care unit. Two pulse oximeters presently on the market, the Ohmeda Biox 3700 and Nellcor N100E, have been assessed separately on normal and critically ill adult patients.^{1–4} These studies showed that both machines are accurate when Sao_2 is above 90%. However, they suggest that the accuracy of the machines at lower saturations is poorer and may exceed the errors claimed by the manufacturers. One study in critically ill children showed a large error (range +8.2% to –9.7%) for one machine (Nellcor).⁵ The aim of this study was to compare the performance of the two machines against simultaneous measurements of arterial oxygen saturation in the same poorly saturated children with congenital heart disease.

Methods

The study was approved by the hospital ethical committee but parental consent was not obtained, since all the patients required indwelling arterial cannulae for management.

Twenty-five children scheduled to undergo surgery for cyanotic congenital cardiac disease were studied. Only those patients whose pre-operative cardiac catheter study revealed Sao_2 less than 90% while breathing air were selected. Patients were excluded if high serum levels of bilirubin were present, since abnormal pigments are known to affect the absorption spectra.

The two pulse oximeters used, the Ohmeda Biox 3700 and the Nellcor N100E, were loaned for the study by the manufacturers. The appropriately sized probes of both machines were attached after induction of anaesthesia, in

accordance with the manufacturers' instructions. The probes were attached either to fingers or to toes, depending on whether a radial or femoral arterial cannula was in place, and on the same limb.

Oximeter readings were recorded as a sample of arterial blood was withdrawn once the output of both pulse oximeters and the patient's cardiovascular variables had been stable for at least one minute. Heart rate, systolic, mean, diastolic and central venous pressures and the core temperature were noted.

Samples of arterial blood and Sao_2 measurements were taken before the initial incision and up to six times after the start of surgery but before cardiopulmonary bypass if planned. Sao_2 was measured immediately by a co-oximeter (OSM-2 Hemoximeter, Radiometer, Copenhagen) and Pao_2 by a blood gas analyser (Instrumentation Laboratory 1306). Both machines were checked and calibrated each day before use but the recorded arterial saturations were not corrected for carboxyhaemoglobin.

Statistical analysis. The sample size of this study was determined by reference to a nomogram relating power, study size, the standardised difference and significance level for a continuous variable.⁶ The sample size should be 25 to achieve a power of 0.8 and a significance level of 0.05 if the manufacturer's specified accuracy is used and a 2.5% error accepted as clinically important.

Estimates of the pooled mean, standard deviation (SD) and standard error of the mean (SEM) were calculated using analysis of variance, since the study involved repeated measurements on the same patient. To examine whether the pulse oximeters differed significantly from each other,

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the data were first transformed to ensure that the variance remained constant over the whole range and then examined by analysis of variance for unequal subsample sizes.⁷ A similar method was used to assess the effect of temperature and haemoglobin level. The regression line of each patient's sample was calculated. Patients were excluded from further calculations if there were less than three samples for a particular patient (patients A, B, C and O) or if the regression coefficient was less than 0.7 (patients D, G, M, R, V and Y). Once no statistical difference between the remaining regression lines was shown, these lines were weighted and pooled by analysis of covariance to provide a single regression line for each machine.

Results

The patients' demographic details and the surgical procedures performed are shown in Table 1. Figure 1 illustrates

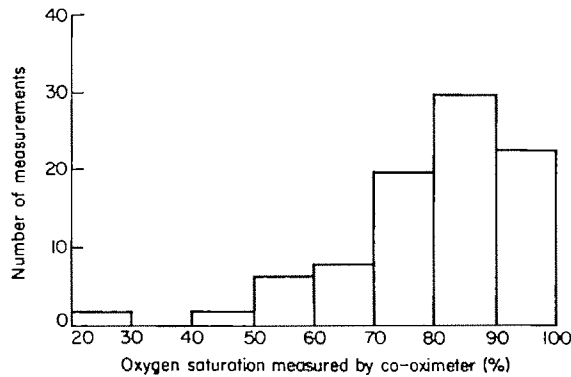


Fig. 1. Distribution of arterial saturation measurements.

Table 1. Demographic details of patients, and surgical procedures.

	Mean (SD)	Range	10th and 90th centiles	
Age, years	2.4 (3.0)	0.01–12.0	0.11	8.1
Weight, kg	10.4 (9.1)	2.62–4.35	2.93	24.2
Haemoglobin, g/100 ml	16.0 (3.2)	11.6–25.1	12.1	20.3
Packed cell volume, %	50 (11)	34–80	37	65

Diagnosis	Surgical procedure	Number of patients
Transposition of great arteries	Arterial switch	3
	Senning	2
	Fontan	1
Tetralogy of Fallot	Blalock–Taussig shunt	3
	Correction	2
	Conduit replacement	1
Pulmonary stenosis or atresia (plus ventriculo-septal defect, small or double-outlet right ventricle)	Blalock–Taussig shunt	5
	Rastelli	1
	Fontan	1
	Repair	1
		1
Other complex congenital heart disease		5

the distribution of the arterial saturations of the patients. A summary of the descriptive statistics concerning the differences between the pairs of saturation measurements is shown in Table 2. The scatter diagrams (Figs. 2 and 3) show the pulse oximeter readings plotted against the reference co-oximeter results in the 25 patients, and the line of identity. Analysis of variance revealed that the two pulse oximeters differed significantly both from each other and from the reference co-oximeter. Further analysis failed to show any

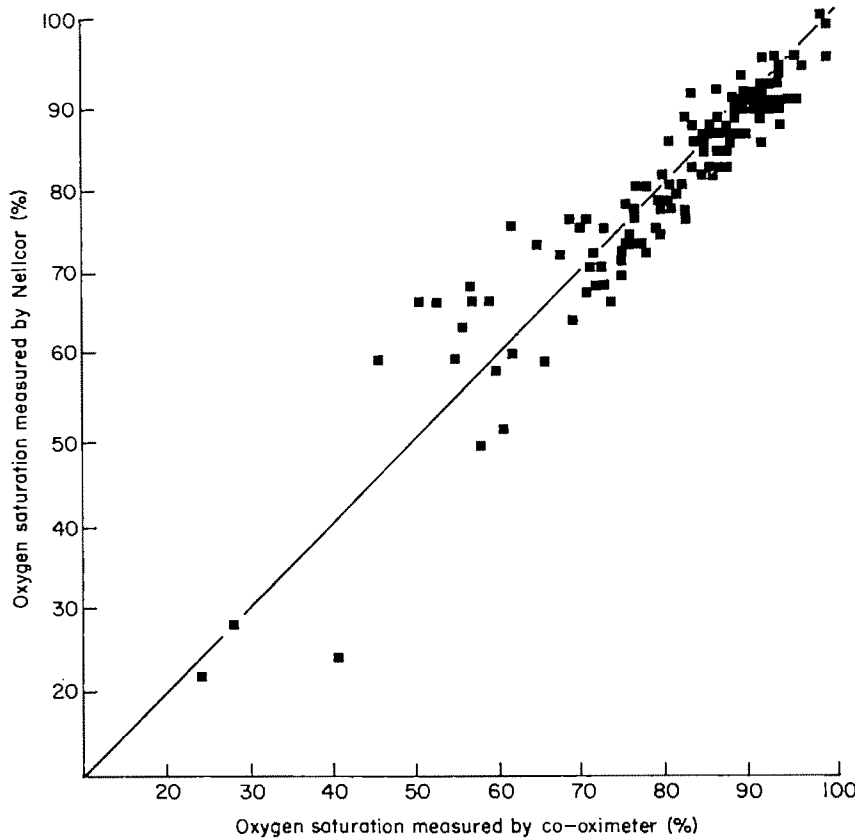


Fig. 2. Scatter diagram of repeated SaO₂ measurements of Nellcor oximeter against co-oximeter for each of the patients (114 data points from 25 patients). Line of identity also shown.

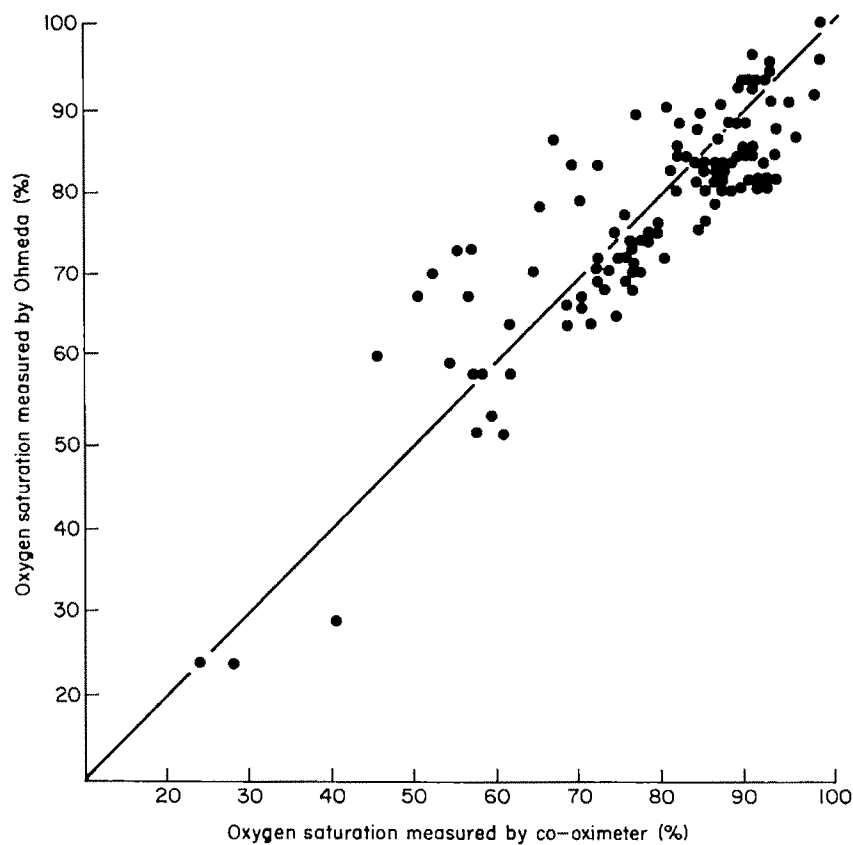


Fig. 3. Scatter diagram of repeated SaO_2 measurements of Ohmeda oximeter against co-oximeter for each of the patients (114 data points from 25 patients). Line of identity also shown.

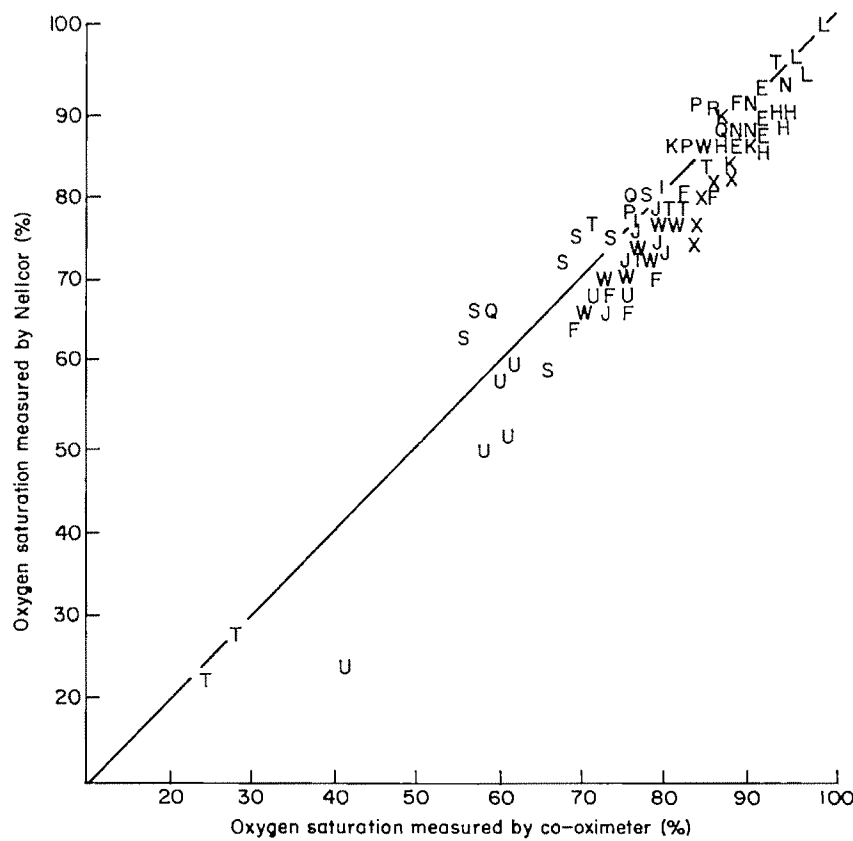


Fig. 4. Scatter diagram of repeated SaO_2 measurements of Nellcor oximeter against co-oximeter for the 15 patients whose data were pooled (patients A, B, C, D, G, M, O, R, V and Y excluded; see text). Line of identity shown.

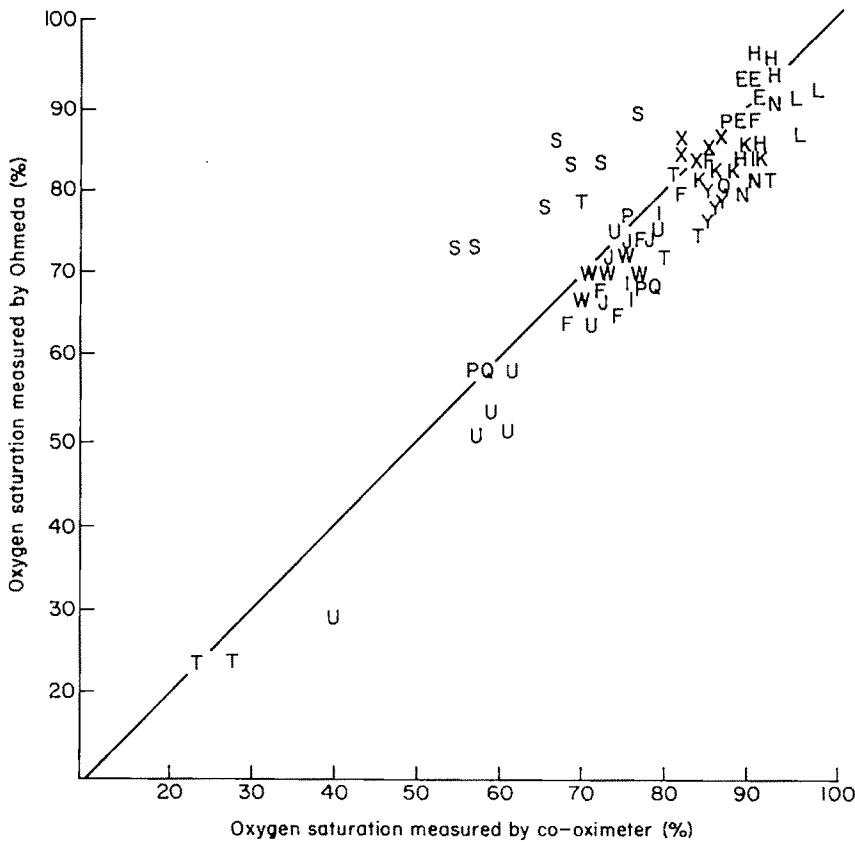


Fig. 5. Scatter diagram of repeated SaO_2 measurements of Ohmeda oximeter against co-oximeter for the 15 patients whose data was pooled (patients A, B, C, D, G, M, O, V and Y excluded; see text). Line of identity shown.

Table 2. Summary of descriptive statistics on difference between pulse oximeter minus reference co-oximeter measurements (%) for both machines.

	Ohmeda	Nellcor
Number of samples	114	114
Range of difference	-13.8 to +17	-18 to +14.8
Centile of difference		
10th	-10	-6.3
90th	+7.6	+4.9
Pooled mean difference (i.e. bias)	-2.8	-0.7
Pooled SD	3.9	3.1
Pooled SEM	2.6	2.0
Pooled/weighted regression line*	$0.97 \times SAT + 2.65$	$1.05 \times SAT - 3.5$
95% Confidence limits of regression line gradient	0.85-1.01	0.97-1.09

* SAT, reference co-oximeter measurement.

significant relationship between the size of the difference between the pulse oximeter and co-oximeter measurements and temperature or haemoglobin concentration. Figures 4 and 5 are scatter diagrams that illustrate only the data from the 15 patients pooled to provide a single regression line.

Discussion

Under the conditions of this study the accuracy of both machines was poorer than the manufacturers' claim for the Ohmeda of $\pm 2.4\%$ and for the Nellcor of $\pm 2.5\%$ over

this range. The performance of these machines during this study was poorer than found in the studies quoted previously;¹⁻⁵ however, these investigations did not assess performance at consistently low SaO_2 . The scatter diagrams show clearly that the variance of the readings of both machines increased markedly below 80% saturation. Both machines differed significantly from each other and from the co-oximeter but the results suggest that the Nellcor performs more consistently and accurately. The Nellcor has a small, constant negative bias over the whole range, while the Ohmeda tends to over-read at low saturations but to under-read at higher saturations.

A positive aspect of both machines is shown clearly in Figs 4 and 5. Where SaO_2 changed markedly during surgery (e.g. patient U), the bias remained constant throughout the range of readings so that changes in SaO_2 were recorded accurately. Surgical diathermy interfered with the function of both pulse oximeters but only the Ohmeda warned of this.

The performance of the pulse oximeters may have been affected adversely by a number of factors.

Temperature. Changes in temperature cause changes in absorption spectra.⁸ In nine patients the central temperature decreased below 36.0°C at some time during surgery. This decrease in temperature combined with conditions of poor perfusion, causes the peripheral temperature to decrease. Thus the arterial blood that perfused the digits under the pulse oximeter probes may well have been cooler than normal (although the peripheral temperature was not measured). The absorption spectrum of reduced haemoglobin is steep at 940 nm, which is one of the wavelengths

used by the Ohmeda machine. Changes in temperature that cause changes in absorption spectra may be expected to have a larger effect on this steep part of the spectrum compared to other, flatter parts such as 925 nm used by the Nellcor machine. This may partly explain the greater variation of the Ohmeda machine. The lack of significance between the errors at central temperatures above and below 36.5°C is difficult to interpret, since large gradients between skin and core temperatures frequently exist during surgery that involves cardiopulmonary bypass. The poor peripheral perfusion of these patients was probably an important cause of the error of the pulse oximeters.

Carboxyhaemoglobin and other pigments. Patients with elevated bilirubin levels were excluded from the study. The presence of carboxyhaemoglobin, however, also causes errors. The carboxyhaemoglobin fraction in the blood of nonsmokers is normally less than 2%⁹ but it is higher in newborns (due to the greater rate of haemoglobin catabolism¹⁰) and city dwellers. All pulse oximeters express saturation as a percentage of functional haemoglobin. Haemoglobin combined with carbon monoxide is effectively nonfunctional and its presence would erroneously elevate the saturation reading given by the machines. This effect is minimal at high oxygen saturation but becomes more significant at lower saturations.¹¹ Unfortunately, the magnitude of the effect of carboxyhaemoglobin on the readings is specified only in the Ohmeda manual; it may differ in other machines and cause greater variation at low saturation.

Haemoglobin concentration. Many patients had a compensatory elevated haemoglobin and consequent increased PCV since they were cyanosed. The increase in haemoglobin should not, in theory, affect the pulse oximeters but Saloojee *et al.*¹² reviewed the performance of the co-oximeter and found that increased haemoglobin levels outside the normal range led to a decrease in the SaO_2 reading. The manufacturer states that the greatest error caused by unusual levels of haemoglobin is under-reading of the true SaO_2 by 1.6% at 100% saturation. Significant errors at low and high haemoglobin concentrations are unlikely, since the variance of the pulse oximeter readings exceeds this. Fetal haemoglobin has an absorption spectrum similar to adult haemoglobin⁸ and so should not bias the machines when they are used in neonates.

In conclusion, these pulse oximeters may be highly inaccurate when used during surgery where SaO_2 changes

rapidly and decreases to low levels. These machines may not be as useful in cyanosed paediatric surgical patients as they are in the management of normal children and adults. They are clinically valuable in that they accurately display trends in SaO_2 in the same patient and can therefore give warning of important changes in saturation.

Acknowledgments

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References

1. CECIL WT, PETTERSON MT, LAMOONPUN S, RUDOLPH CD. Clinical evaluation of the Biox IIA Ear Oximeter in the critical care environment. *Respiratory Care* 1985; **30**: 179–83.
2. TWEEDDALE PM, DOUGLAS NJ. Evaluation of Biox IIA Ear Oximeter. *Thorax* 1985; **40**: 825–7.
3. TYTLER JA, SEELEY HF. The Nellcor N101 pulse oximeter. *Anaesthesia* 1986; **41**: 302–5.
4. YELDERMAN M, NEW W. Evaluation of pulse oximetry. *Anesthesiology* 1983; **59**: 349–52.
5. FANCONI S, DOHERTY P, EDMONDS JF, BARKER GA, BOHN DJ. Pulse oximetry in pediatric intensive care; comparison with measured saturations and transcutaneous oxygen tension. *Journal of Pediatrics* 1985; **107**: 362–6.
6. GORE SM. How large a sample? In: GORE SM, ALTMAN DG, eds. *Statistics in practice*. London: British Medical Association, 1982: 6–8.
7. SNEDCOR GW, COCHRAN WG. *Statistical methods*, 6th edn. Iowa: Iowa University State Press, 1967: 259–98.
8. SIGGARD-ANDERSEN O, NØRGAARD-PEDERSEN B, REM J. Hemoglobin pigments. Spectrophotometric determinations of oxy-, carboxy-, met-, and sulfhemoglobin in capillary blood. *Clinica Chimica Acta* 1972; **42**: 85–100.
9. COLLIER CR. Oxygen affinity of human blood in presence of carbon monoxide. *Journal of Applied Physiology* 1976; **40**: 487–90.
10. FALLSTROM SP. On the endogenous formation of carbon monoxide in full-term newborn infants. *Acta Paediatrica Scandinavica* 1969; **58** (Suppl.): 189.
11. REM J, SIGGARD-ANDERSEN O, NØRGAARD-PEDERSEN B, SØRENSEN S. Hemoglobin pigments. Photometer for oxygen saturation, carboxyhemoglobin and methemoglobin in capillary blood. *Clinica Chimica Acta* 1972; **42**: 101–8.
12. SALOOJEE Y, COLE PV, ADAMS L. The evaluation of a photometer (the Radiometer OSM2) for the determination of haemoglobin concentration and per cent oxyhaemoglobin and carboxyhaemoglobin in blood. *Journal of Medical Engineering and Technology* 1981; **5**: 298–300.

The Ruben circle anaesthesia system

An investigation of reverse flow of patient expired gas during spontaneous breathing

M. J. SIK, D. J. EVELEIGH AND R. B. LEWIS

Summary

The Ruben circle anaesthesia system was studied in the spontaneous breathing mode, and under certain conditions there was incompetence of the replaceable mushroom control valve. This causes a reverse flow of gas which results in rebreathing of expired gas when the system is used on spontaneously breathing patients. A patient simulator was used to investigate the way in which the reverse flow of gas depends on ventilatory parameters and fresh gas flow. The inspired concentration of carbon dioxide increased for increased fresh gas flow and for decreased tidal volume. These results were confirmed by observations on anaesthetised adult and paediatric patients during spontaneous breathing. We conclude that the system in its present form, is not suitable for use on spontaneously breathing paediatric patients.

Key words

Equipment; circuits, Ruben circle anaesthesia system.

An anaesthesia system which eliminates the need for adjustment of the overflow valve was described by Ruben.¹ A system based on this design is manufactured by Ambu International, Copenhagen, Denmark and was recently introduced onto the British market under the name of the Ruben circle anaesthesia system (Fig. 1). Reports received

in the patient's inspired gas. It was reported that the degree of rebreathing depended on the fresh gas flow introduced into the system and that the concentration of carbon dioxide increased with increased fresh gas flow.

We tested a Ruben circle system in order to investigate this effect and to establish the cause, using a simulated spontaneously breathing patient. This enabled the system to be tested conveniently and reproducibly for varying conditions of ventilation which could be defined precisely. The results were confirmed by observations on anaesthetised adult and paediatric patients who breathed spontaneously.

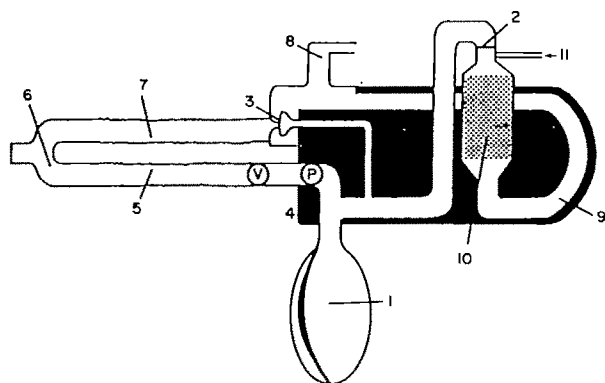


Fig. 1. The Ruben circle anaesthesia system. 1, Reservoir bag; 2, expiratory valve; 3, control valve; 4, inspiratory valve; 5, inspiratory tube; 6, patient Y-piece; 7, expiratory tube; 8, spill valve; 9, expiratory reservoir; 10, absorber; 11, fresh gas inlet.

by the Scottish distributor of the system indicate that conventional capnography in spontaneously breathing adult patients has demonstrated the presence of carbon dioxide

Methods

Simulated conditions were generated by means of a modified Starling pump. This system has been tested on conventional breathing systems and shown to simulate accurately, spontaneously breathing patients. It enables tidal volume and frequency to be varied in a controlled way. The inspiratory:expiratory (I:E) ratio is fixed at 1:1.7 and the system incorporates a functional residual capacity and deadspace. It is possible to introduce physiological flows of carbon dioxide in order to demonstrate the effect of variations in the breathing system on inspired and expired carbon dioxide concentrations. Tracings of flow pattern and carbon dioxide concentration at

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the outlet of the patient simulator are shown in Fig. 2(a) for a tidal volume of 250 ml, a frequency of 20 breaths/minute, a deadspace of 60 ml and carbon dioxide production of 170 ml/minute.

The operating principles of the Ruben circle system indicate that the most likely reason for the appearance of carbon dioxide at the patient connexion during the inspiratory phase would be leakage at the control valve (3 in Fig. 1). This would permit reverse flow along the expiratory tube during at least part of the inspiratory phase. In order to demonstrate this effect, a calibrated pneumotachograph head (Mercury Electronics F100L) was inserted directly on the patient side of the control valve. In this position the pneumotachograph provides a sensitive indication of reverse flow. A capnograph was also connected to the system with the sampling point at the connexion to the patient Y-piece, in order to demonstrate the presence of carbon dioxide at the patient connexion during the inspiratory phase.

A Mercury Electronics Model CS5 electrospirometer was used to obtain flow measurements and a Datex Normcap Model CD102 carbon dioxide analyser for capnography. The electrospirometer allowed quantitative measurements of flow and, by integrating the flow over a relevant time interval, a corresponding volume could be obtained. These quantitative measurements were undertaken only with the system connected to the patient simulator. It was therefore necessary to calibrate the measuring system at only one gas composition (95% oxygen/5% carbon dioxide) and it was also possible to use the stroke volume of the patient simulator for a direct calibration of flow and volume. The linearity of response for the pneumotachograph over the range 0–30 litres/minute was first checked and found to be within the manufacturer's specification of within 5%. The pneumotachograph was then connected to the outlet of the patient simulator which was set to a known stroke volume. Calibration of both volume and flow was obtained directly from the flow tracing and it was established that these measurements could be obtained with an accuracy better than within 10%. The capnograph was calibrated against a standard calibration gas (BOC Hy-line: 4.8% carbon dioxide, 12.0% oxygen, 83.2% nitrogen). The accuracy of

measurement was within 0.1% when used with the patient simulator; in the clinical situation the accuracy reduces to within 0.2% because it is necessary to switch in the nitrous oxide compensation. It was intended to measure low levels of rebreathing so particular attention was paid to zero drift and to offsets introduced by high concentrations of nitrous oxide. Zero stability was maintained to within 0.1%. The response time of the capnograph was 400 milliseconds for a 0–90% response.

The control valves of the Ruben circle system are demountable and plug into the relevant port on the main circle system housing. The valve position is well defined when the valve is pushed firmly into the port although it may be rotated. The valves are clearly intended to be axially symmetric and the rotational position should be irrelevant. We tested the circle system with seven separate control valves using the patient simulator. One valve (valve 1) had previously been used for an unknown time; the other six were unused.

In order to confirm that effects demonstrated with the patient simulator take place when the system is used in clinical practice, we used the circle system on a series of seven adult patients and in one paediatric case. Conventional capnography was used in all cases and flow analysis for the adult patients was undertaken with the pneumotachograph head connected directly on the patient side of the control valve, as described above. Control valve number 2 was used for all clinical studies.

Functional and leak checks were undertaken as recommended by the manufacturer, before the circle system was used either with the patient simulator or in clinical practice.

Results

A reverse flow during the inspiratory phase was demonstrated for six of the seven valves tested on the patient simulator, with a corresponding indication of carbon dioxide at the patient connexion. The magnitude of the effect was different for each valve tested and for one valve the effect depended on the rotational position and was accurately reproducible as the valve was rotated.

Typical tracings of flow measured by the pneumotachograph

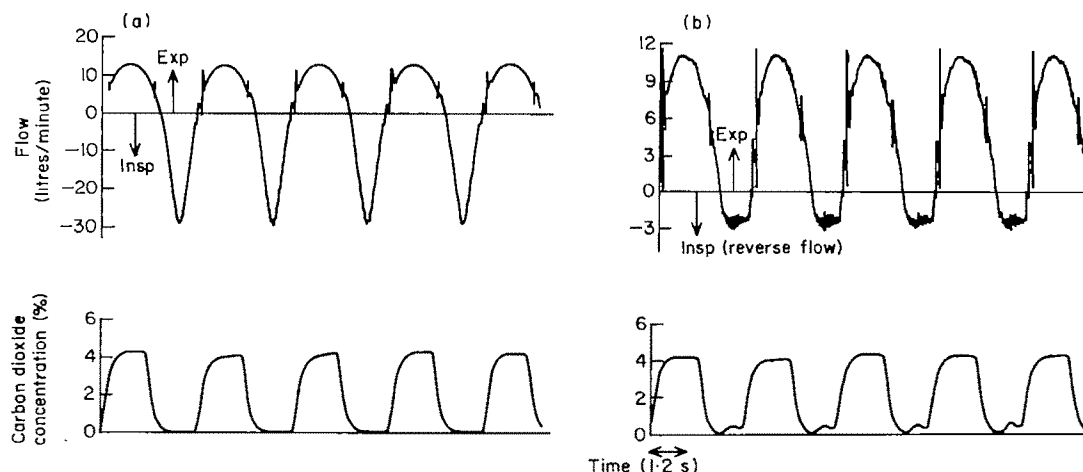


Fig. 2. (a) Flow pattern and carbon dioxide concentration at the outlet of the patient simulator with no anaesthetic breathing system connected. The settings were tidal volume 250 ml, frequency 20 breaths/minute, deadspace 60 ml, carbon dioxide production 170 ml/minute. (b) Flow pattern in the expiratory tube of the Ruben circle and carbon dioxide concentration at the patient Y-piece for simulated respiration. Control valve number 2 was used in the Ruben circle with a fresh gas flow of 2 litres/minute. The simulator settings were as in (a).

graph and corresponding carbon dioxide levels at the patient Y-piece are shown in Fig. 2(b). These tracings were obtained for valve 2 with a tidal volume setting of 250 ml, frequency 20 breaths/minute, carbon dioxide production 170 ml/minute and fresh gas flow 2 litres/minute. A clear indication of reverse flow during the inspiratory phase is seen in the flow tracing together with the presence of carbon dioxide during part of the inspiratory phase.

The total volume of gas that flows in the reverse direction along the expiratory limb during the inspiratory phase can be obtained by integration of the reverse flow. Table 1

Table 1. Volume of gas that flows in the reverse direction along the expiratory tube during each ventilatory cycle of the patient simulator.

Valve number	Reverse flow volume/breath (ml)
1	9
2	34
3	38
4	36
5	31
6	9.5
7	0

The settings used to test each valve were tidal volume 250 ml, frequency 20 breaths/minute and fresh gas flow 2 litres/minute.

summarises these results for the seven valves tested, with tidal volume maintained at 250 ml, frequency 20 breaths/minute and fresh gas flow 2 litres/minute. The results, which refer to different valves used under identical conditions of simulated spontaneous respiration, show that the reverse flow depended on the control valve that was used. The performance of the circle system was compromised for six of the seven valves tested.

We also used the patient simulator to investigate the way in which the reverse flow depended on ventilatory parameters and fresh gas flow. The volume of gas that flowed

in the reverse direction depended strongly on the introduced fresh gas flow but was almost independent of tidal volume. For valve 2 the variation of reverse flow with fresh gas flow is shown in Table 2 for tidal volumes of 250 and 70

Table 2. Volume of reverse flow for different settings of fresh gas flow.

Fresh gas flow (litres/minute)	Reverse flow volume/breath (ml)	
	Tidal volume 250 ml	Tidal volume 70 ml
0.3	6	7
0.5	9.5	11
1.0	16	19
2.0	30	35
3.0	44	47
4.0	53	56
6.0	73	64
8.0	83	—

These results were obtained using valve 2, with frequency set to 20 breaths/minute for both settings of tidal volume.

ml, in each case for a frequency of 20 breaths/minute. The results indicate that the reverse flow has greatest clinical significance for small tidal volumes and high fresh gas flows. The effect was also illustrated by using the patient simulator at relevant settings. Figure 3 shows the results for settings which are appropriate for a 10-kg child, which is the recommended lower limit for use of the system (tidal volume 70 ml, frequency 27 breaths/minute, deadspace 20 ml, carbon dioxide production 70 ml/minute). The sequence of tracings shows the effect of increased fresh gas flow. The concentration of inspired carbon dioxide increases significantly as the fresh gas flow is increased and would be clinically significant for this setting of tidal volume.

Observations on spontaneously breathing patients showed that reverse flow was present in all adult patients and that its magnitude increased for increased fresh gas flow. The significance of the resultant rebreathing in terms of the inspired and expired carbon dioxide concentrations, obviously depends on the patient's tidal volume. The effects

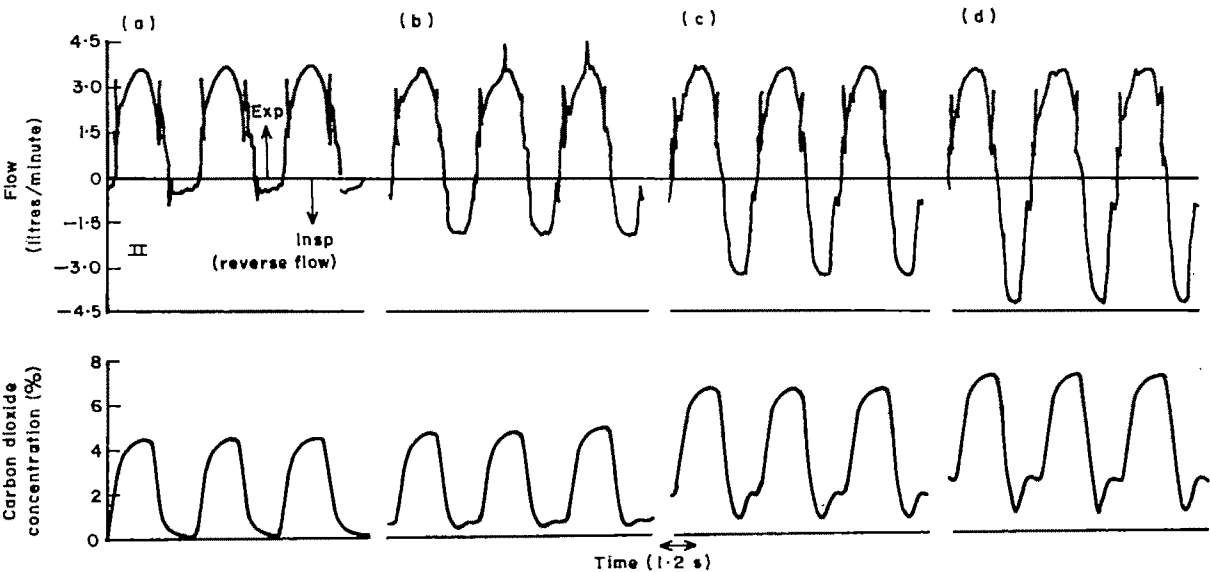


Fig. 3. Effect of increasing fresh gas flow for a paediatric setting on the patient simulator, i.e. tidal volume 70 ml, frequency 27 breaths/minute, deadspace 20 ml, carbon dioxide production 70 ml/minute. Tracings of flow in the expiratory tube and carbon dioxide concentration at the patient Y-piece are shown as a function of fresh gas flow: (a) 0.3 litres/minute; (b) 1.5 litres/minute; (c) 3 litres/minute; (d) 4 litres/minute.

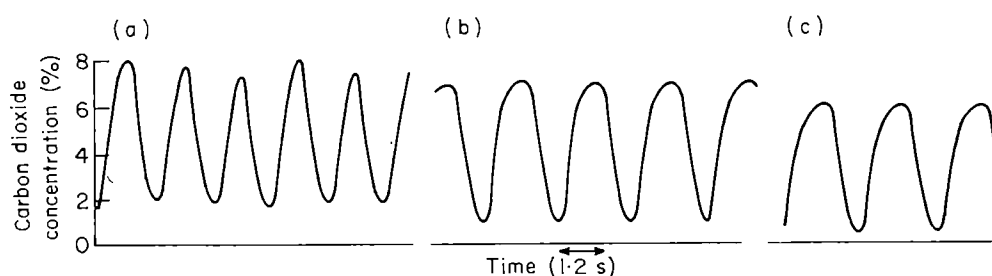


Fig. 4. Carbon dioxide concentration at the airway of a spontaneously breathing, anaesthetised adult patient connected to the Ruben circle. The variation of carbon dioxide concentration is shown for three settings of fresh gas flow: (a) 6 litres/minute; (b) 2 litres/minute; (c) 0.5 litres/minute.

demonstrated with the patient simulator were present, as shown in Fig. 4, although they are of little clinical significance in most adult situations; these results refer to a 24-year-old, unpremedicated male patient undergoing removal of a lump on the foot. Gas sampling was undertaken at an airway beneath a facemask which was used with the Ruben circle. Some gas mixing occurs beneath the mask, as is evident from the shape of the tracing, but the important feature of the tracing is the variation of the inspired carbon dioxide concentration for different fresh gas flows. Increase of the fresh gas flow increased the level of inspired carbon dioxide.

Measurements on adult patients also showed significant changes in the flow pattern during expiration for different fresh gas flows. We did not investigate this in detail but it appears to occur because the pressure in the expiratory tube during expiration depends on the fresh gas flow. This would be expected to a certain extent, because of the dynamic resistance of the spill valve. However, at high fresh gas flows, dumping of gas through the spill valve occurs before the end of the expiratory phase. An increase in pressure in the expiratory tube is caused by partial inflation of the control valve (3 in Fig. 1).

The problems that arise from reverse flow are more significant for small tidal volumes. To demonstrate an extreme case, we used the circle system for a very brief period on a 10-month-old child who weighed 11.9 kg. The child, who breathed spontaneously, was intubated and gas samples were taken from a connexion on the suction port of a Magill armoured tracheal tube. An Ayre's T-piece was used in the normal way for most of the operation but the Ruben circle system was substituted for brief periods. Figure 5

shows tracings of carbon dioxide concentration for various fresh gas flows using the Ruben circle. The limitations of the response time of the capnograph are apparent on the trace but the very significant effect on the inspired and expired concentrations of carbon dioxide is obvious. Because of the magnitude of the effect we did not pursue the investigation of clinical paediatric cases, since the results obtained with the simulator clearly demonstrated the effects to be expected.

Discussion

We did not attempt a full assessment of the performance of the Ruben circle system but addressed the specific problem of reverse flow during spontaneous breathing. This is caused by limitations in the action of the control valve and there was considerable variability in the efficacy of different valves tested.

The Ruben circle would normally be used with low fresh gas flows as a semiclosed or closed breathing system. Under these circumstances the reverse flow may have little clinical significance with adult patients. However, reverse flow increases with increased fresh gas flow and the instinctive reaction to increase fresh gas flow in order to reduce rebreathing would only exacerbate the problem. The effect is more important at small tidal volumes. This has significant implications for use of the system in paediatrics and, indeed, for adult patients with respiratory depression. We do not consider that it is safe to use this system for spontaneously breathing paediatric patients until suitable steps are taken to improve the performance of the control valve.

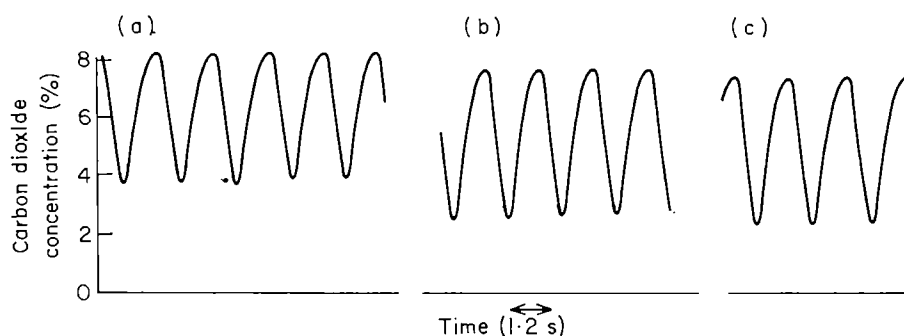


Fig. 5. Carbon dioxide concentration at the tracheal tube of an anaesthetised, spontaneously breathing child, weight 11.9 kg. The variation of carbon dioxide concentration is shown for three settings of fresh gas flow: (a) 3 litres/minute; (b) 2 litres/minute; (c) 0.6 litres/minute.

Editor's note

The manufacturers, partly as a result of this study, have recognised the problem and modified the seat of the valve to be larger in diameter and higher. It has also been modified to prevent distortion during storage. The authors are testing the modified valve system.

Reference

1. RUBEN H. Anaesthesia system with eliminated spill valve adjustment and without lung rupture risk. *Acta Anaesthesiologica Scandinavica* 1984; **28**: 310-4.

HISTORICAL

The appointment of an anaesthetist

Edinburgh Royal Infirmary 1900–12

A. H. B. MASSON

Summary

This is an historical vignette about a stage in the evolution of specialist anaesthesia in the capital city of Scotland. Ignorant management decisions delayed development in Edinburgh by 25 years.

Key words

Education; medical students.

History.

The first anaesthetists in Edinburgh were in the Dental Hospital. William Guy, who was much interested in anaesthesia, was appointed as Dean of the Edinburgh Dental School in 1899 and, by the following year, the Dental Hospital had several anaesthetists who attended on a sessional basis. They agreed in October that 'anaesthetics should only be administered in the hospital by or under the direction and in the presence of a qualified medical practitioner.'

The first anaesthetist in a surgical hospital was Dr. D. C. A. McAllum who was appointed to the Royal Hospital for Sick Children in 1900. His appointment was requested by (Sir) Harold Stiles, surgeon at the hospital, who wrote to the Board of Management: 'I have frequently had to solicit the services of any qualified man who chanced to be attending the hospital and I have often been obliged to fall back upon a senior student. In the Royal Infirmary, the anaesthetic is administered by a junior House Surgeon.' The Board, however, 'wish it to be understood that the appointment of a special anaesthetist should not prevent any qualified member of the staff from administering an anaesthetic'. Dr Thomas D. Luke was appointed anaesthetist to the Deaconess Hospital later that year.

The first letter

These appointments had some effect on the surgeons of the Royal Infirmary. A letter early in October 1901, from a Dr Barry Hart was considered by the Medical Managers' Committee of the Infirmary. It read:

'Dear Dr Muirhead,

For some time past, I have been strongly impressed with the desirability of the Royal Infirmary having special and qualified anaesthetists attached to the staff. The

traditions of our school have been for the anaesthetics to be given by senior students but the time seems to me to have come for a modification of this arrangement. Fresh methods of anaesthetising have come into vogue, operations requiring prolonged administration are much more common and special arrangements for slight or short anaesthesia are now much practised. The responsibility of a prolonged operation is a great strain both on the student and operator and the newer methods are not uniformly taught.

Now if two or three specially qualified anaesthetists were appointed to our Infirmary, the advantages would be as follows. For serious operations, the operator would have the advantage of a specially skilled anaesthetist who would not only give the drug more safely and with less risk of distressing subsequent sickness but would take off the operator's shoulders the responsibility of the administration. This in itself is a formidable operation is no small boon. Then the anaesthetist would be able to give the students special and uniform instruction in anaesthetising at first in theory and afterwards by actual trial under their superintendence. It would be a great advantage for students many of whom go to England or abroad to have special instruction in the administration of ether by apparatus and in the methods practised by dentists.

I do not for one moment propose to take from our students the privilege of anaesthetising; indeed, owing to the extent to which anaesthetics are used daily in the Infirmary, this would be impossible; but only that uniform instruction be given, careful supervision of their first trials be exercised and the responsibility of serious or prolonged cases taken by a specially qualified man.

I would be greatly obliged if you would give this matter your consideration.'

The Managers passed the letter to the Surgical Staff Committee which consisted of all the senior surgeons. They met

in Mr Annandale's house on 18 October 1901 with Annandale in the Chair. Annandale was Regius Professor of Clinical Surgery, having succeeded Lister in 1877. Of the 10 surgeons present, seven, including Annandale and the Professor of Surgery, John Chiene, spoke in favour. Three were against.

Mr (later Sir David) Wallace 'was strongly opposed to the appointment of special anaesthetists. He doubted if greater safety would accrue in the giving of anaesthetics, more especially since fatalities occurred in minor or trivial cases, not in the more prolonged and serious operations. He did not think it would be practical to command the services of a special anaesthetist more especially at emergency operations and if any appointment were made he hoped the duties would be simply those of an instructor.'

Francis Caird, who succeeded Annandale as Regius Professor of Clinical Surgery in 1908, 'considered such an appointment objectionable. It would reflect on the members of the staff as having neglected their duty in giving suitable instruction to those whom they have permitted to anaesthetise the patients under their care. It shifted responsibility and he was of opinion that when fatalities occurred it would be found that there was a dual control during the administration of the drug, no one being personally responsible. It would cause a serious loss of confidence in the relations between the staff and their patients and above all would lay those surgeons who could not obtain or did not desire the services of the special anaesthetist open to blame and question. And once this disturbing element were introduced, there would be an end to the suitable education of the medical student and the anaesthetist's services would be almost obligatory in every case'.

Mr MacGillivray was 'strongly opposed to any such appointment. He considered it his duty to teach and train his students and he had had no fatalities. He did not think the services of a 'sporadic' anaesthetist desirable and the appointment of six anaesthetists was impracticable'. (There were six surgical charges in the Infirmary.)

The November meeting of the Board was informed that 'a conference has since been held by the Medical Management Committee with members of the Surgical Staff when it was agreed practically unanimously (*sic*) that an Instructor on the administration of anaesthetics should be appointed whose duty it would be to teach the students the proper method of administering chloroform, ether, etc. and who would be allowed to give practical demonstrations of administering anaesthetics where necessary in minor operations which are performed from time to time by the Resident Surgeons but also would not be entitled to take part in major operations'. (The anaesthetics for these would, presumably, continue to be given by the junior house surgeons.) 'The Instructor, however, would also be empowered to grant a certificate to students which would be a requisite for all resident posts'. This was a considerable advance considering the fact that, prior to this, no formal instruction in anaesthesia had been given to student or to resident. However, only a month later, the significance of the words 'practically unanimously' became apparent. The minutes then recorded that the surgeons 'did not desire the appointment of an anaesthetist who would be at liberty to demonstrate anaesthetics'. What they wanted was 'merely a teacher on the subject'. The Board decided that, since it was a teacher they wanted and not an anaesthetist, it was a matter for the University and not for them. With that, the

first attempt to get an anaesthetist on the staff of the Infirmary ended.

Luke, as instructor

Luke's sponsor and protagonist for his appointment to the Deaconess Hospital was Annandale, who tried to have him appointed to the Royal Infirmary. Thwarted by the decision recorded above, Annandale now wrote to the Board requesting that Luke be appointed as Instructor. 'He is,' Annandale wrote, 'a thoroughly skilled and experienced anaesthetist (who) will not in any way interfere with the patients (!) or their treatment (but) simply give tutorial instruction to my class. Remuneration will be arranged by myself'. The Board agreed and, at the same time, McAllum was appointed Anaesthetic Instructor to Cathcart. Annandale notified the Faculty of Medicine of Luke's appointment and the University Senate in May 1902 approved a form of certificate to be given to students in the class of clinical surgery, or to those students who chose to attend, for Luke's classes were optional. The certificate required attendance at at least four of the six lectures and the personal administration under supervision of not less than 10 anaesthetics. The classes were popular and well attended and, 2 years later, Luke was appointed Lecturer with a salary of £50 *per annum*. The Senate minute read: 'During these three years, Dr Luke has given such instruction with much success and the Faculty, impressed with the importance of such instruction, now desire to extend it so as to include all students in the University wards of the Royal Infirmary.'

Luke's position in the Infirmary was, however, very difficult. He had no official standing and had to apply annually for re-appointment. When he complained in 1906 that it was impossible to carry out his duties as a Lecturer without access to the wards, the Managers replied that they 'had already agreed to extend Dr Luke's term of office for three months beyond the five years laid down in the Rules'. The rules concerned the appointment of clinical tutors, trainee posts for surgeons and physicians roughly equivalent to today's senior registrars. But, 'for the convenience of Professor Annandale' he was re-appointed for one year. However, the Managers were adamant on the question of access to patients. Luke's post was a supplementary one. 'As a rule, such instruction (i.e. in anaesthesia) is given by the Clinical Tutors. A proposal for the appointment of an anaesthetist was brought forward in the year 1901 but, after consultation with the surgical staff, it was ascertained that such an appointment was not desired by that body.'

The second letter

Not all the surgeons shared that opinion. No fewer than 30 members of the surgical staff (one would have thought a considerable majority) then wrote asking that Luke and McAllum be appointed as Instructors in *practical* anaesthesia on a 5-year term with the same privileges as the physicians and surgeons on the staff, but this was categorically refused. The opposition may have been small in numbers but it was clearly very powerful. Luke and McAllum, senior though they were, were to remain classified as supernumerary clinical tutors but, unlike them, they were excluded from contact with patients. Luke was totally dependent on Annandale's support and his position was

untenable when Annandale died in December 1907. Bereft of support, his frustration and anger boiled over in a bitter, frank and indiscreet letter which was published in the *Lancet*.¹ After criticising surgeons and their 'hidebound prejudice and unwillingness to accept any sort of reform or progress' and 'a determination not to allow anyone or any circumstance to detract from the supremacy and magnificence of the surgeon', he concluded: 'It would be unfair and ungenerous of me in the extreme if I did not freely and gratefully acknowledge that there are many surgeons who welcome one's presence at an operation and readily admit their disinclination, nay their incapacity, to take charge of the anaesthetic as well as to carry out some grave surgical operation or indeed a comparatively trivial one' . . . 'In the Edinburgh school, the late Professor Annandale was the first to recognise the clamant necessity of proper instruction of students and in view of his seniority all honour to him. On the lines laid down by him six years ago, teaching has since been conducted in the Royal Infirmary so far as his wards are concerned'.

Annandale was succeeded by Caird, who had expressed his strong opposition to anaesthetists at the meeting in 1901. He and Professor Chiene now 'both expressed their unwillingness to permit Dr Luke to give practical instruction in their wards'. Luke gave up anaesthesia and moved to the Hydropathic Institute at Peebles as resident physician. His departure was a great loss to anaesthesia and to Edinburgh for he was an enthusiastic and dedicated teacher who wrote two small textbooks and was a frequent contributor at local society meetings.

National pressure

The 'clamant necessity' for proper instruction of students was a theme that was strongly advocated about this time by Buxton, Hewitt and others. Hewitt played a leading role in having a Bill, *The Anaesthetics Bill*, introduced to the House of Commons on 22 June 1909. The preamble stated that: 'the object of the Bill is to require a medical practitioner or a dentist applying for registration on or after 1 January 1912 to submit evidence of having received practical instruction in the administration of anaesthetics and to prohibit any person not a registered medical practitioner or registered dentist administering an anaesthetic.'

The General Medical Council, in its educational role, had to take notice. It appointed a committee to consider the proposals for legislation which 'had been or might hereafter be put forward'. The Council agreed with the object of the Bill and its Education Committee introduced a requirement that instruction must be given to all students in the form of lecture demonstrations and the practical administration of anaesthetics under supervision. It was ironic that Luke, who had done so much in this regard, had at exactly this time been eased out of anaesthesia and of Edinburgh.

The minutes of the meeting of the Faculty of Medicine on 1 December 1908 record that a letter from Dr Luke, Lecturer in Anaesthesia, was read. The contents are not stated but the demand for his resignation was the probable subject. The next item in the minutes was that 'the Dean referred to the terms of a proposed Bill dealing with anaesthetics and the attitude of the GMC on the subject'. The minute went on: 'In view of a letter received from the GMC and the probability of this question being specifically

inquired into and reported upon by the Inspectors of the Medical Council, the Faculty appointed a committee to consider the subject'. The two they appointed were Caird and Chiene. There was no anaesthetist on the committee.

One might have presumed that the only reason why such strenuous efforts were made to exclude anaesthetists from the Infirmary, would have been that others did the job better. Be that as it may, the standard was not high as the trail of deaths under anaesthesia bears witness. It became compulsory in 1905 to report these to the Procurator Fiscal and thereafter, the Infirmary minutes include, for example, 'died while being chloroformed in preparation for an operation for whitlow', 'died following a minor operation', 'died having his varicose veins operated on' and so on. In every instance, however, the Medical Managers 'were satisfied that all ordinary precautions were taken and that no blame attached to anyone' (except perhaps the patient for being unduly susceptible.) Following the deaths of two children having minor surgery, it was minuted: 'With regard to the general question of deaths under anaesthesia, the committee after discussion agreed to report that, looking to the number of serious operations now performed, the number of fatalities was not greater than had been recorded on average for a considerable number of years past'.

The third letter

In 1911, after the death under anaesthesia of an 8-month-old child, the Fiscal wrote a very critical letter to the Board of Management of the Infirmary which ended: 'Crown Counsel are of opinion that in operations of a major character which are not urgent, it is advisable that every precaution with reference to the observation and preparation of the patient prior to operation should be used and particularly with the practice of a public institution such as the Royal Infirmary'. The letter was brought to the notice of the Surgical Staff, who wrote to the Managers: 'The Surgical Staff would be obliged if you would kindly communicate the following resolution to the Managers of the Royal Infirmary: That the Surgical Staff believe that, in the interests of the Institution, the assistance of officially recognized anaesthetists should be obtained'.

That was the third such request in 11 years. The Managers considered the letter and replied that 'this communication raised a very important and far reaching question', 'that it would require very careful consideration in view of the fact that there might be legislation shortly on the administration of anaesthetics' (although the Bill never did become law), 'and that, should the suggestion of the staff be carried out, it would in all probability involve the Institution in expense in the shape of salaries'. The results of their careful consideration came on 18 March 1912. 'They recognised that in the Surgical Wards it is not always possible to ensure that a qualified medical man is available to devote his whole attention to and to directly supervise the administration of anaesthetics and that it is desirable in the interests of the patient that this precaution should always be adopted. The Committee is of opinion that such assistance should be afforded to each Surgical Charge as well as in the Out-patient Department and therefore recommend that the seven clinical tutors (surgeons in training!) who at present have no official status on the staff of the Infirmary should be appointed to supervise the administration of anaesthetics

at an annual honorarium of £15 each—a figure increased immediately to £20. In spite of the brave preamble, they not only ratified the *status quo ante* but rewarded the surgeon for supervising the student while he was operating.

More than 25 more years were to pass before an anaesthetist in the Royal Infirmary of Edinburgh was recognised as a member of the Honorary Staff.

Acknowledgment

The author wishes to thank Miss Lesley De Jean, archivist

to the Lothian Health Board and to the Royal College of Surgeons of Edinburgh, for her help, the Lothian Health Board for permission to quote from the minute books of various Edinburgh hospitals, and the University of Edinburgh to quote from the minutes of the Faculty of Medicine.

Reference

1. LUKE TD. Coroners' Inquests upon deaths in surgical anaesthesia. *Lancet* 1908; 1: 1107–8.

Forum

AIDS in ICUs: outcome

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Summary

*The admission of patients with acquired immune deficiency syndrome (AIDS) to intensive care units in the United Kingdom was surveyed in January 1986. Ninety-three intensive care units completed the questionnaire. Thirty-two patients had been admitted to 12 units up to that time. Twenty-five (78%) of these patients had received artificial ventilation of the lungs. The commonest cause of respiratory failure on admission was *Pneumocystis carinii* pneumonia; this occurred in 27 patients, seven of whom also had pulmonary cytomegalovirus infection. Four patients had Kaposi's sarcoma and three of these patients also had *Pneumocystis carinii* pneumonia. The overall mortality was 72%; twenty (80%) of the patients who required artificial ventilation, died. Ten patients survived to leave the intensive care unit, but one patient died of respiratory failure prior to discharge home.*

Key words

Complications; acquired immune deficiency syndrome. Intensive care.

The incidence of acquired immune deficiency syndrome (AIDS) in the United Kingdom continues to increase. However, the role of intensive care in the management of patients with AIDS-related conditions has not been delineated and there is a wide range of opinion as to the efficacy of aggressive management of serious complications. A survey was therefore carried out to determine how many patients had been admitted to intensive care units (ICUs) in the United Kingdom, and the outcome of treatment.

Materials and methods

A questionnaire was sent to a total of 124 ICUs in the United Kingdom. The questions (Table 1) were designed to obtain basic information about the diagnosis on admission, and the outcome.

Results

Ninety-three units (74%) replied to the questionnaire and of these, 12 units had admitted a total of 32 patients with AIDS. The average age of the patients was 37 years, and all were male. Ten patients were discharged from the ICU and, of these, nine were discharged home. One patient was discharged from the ICU but relapsed and died unexpectedly. The overall mortality was 72%.

The reason for admission of 27 patients was respiratory failure due to *Pneumocystis carinii* pneumonia (PCP). PCP was confirmed in 24 patients, and presumed from typical clinical and radiological features in the remaining three. Seven patients with PCP also had infection with cytomegalovirus. One patient was admitted with aspiration pneum-

Table 1. Information sought in questionnaire.

Age
Antibody status
Admission diagnosis
Presence of concomitant disease
Requirement for artificial ventilation
Outcome
Cause of death in nonsurvivors
Duration of period between start of active treatment and admission to ICU
Administrative policy in respect of nursing and allocation of equipment

onia; this patient had Christmas disease. Other causes of admission were cardiac toxoplasmosis, cerebral toxoplasmosis, toxic megacolon and Kaposi's sarcoma with pulmonary involvement.

Artificial ventilation of the lungs was required in 25 patients (78%); five of these patients survived. Of the survivors, one patient had Kaposi's sarcoma without PCP, and the other four had PCP. Three patients with Kaposi's sarcoma and PCP died. Of the seven patients who did not require artificial ventilation, four survived. Three of these patients had PCP, and one was admitted with cardiac dysrhythmias; two patients admitted with PCP, and one with toxic megacolon, died.

A total of 23 patients died; one patient was reported to have died as a result of toxic megacolon, and the remaining 22 from respiratory failure. Septicaemia was given as an alternative cause of death in five of the patients with respiratory failure.

Correspondence should be addressed to Dr N. Soni please.

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All patients were nursed in isolation rooms. All patients had positive antibody tests. The ICU pool ventilators were used in nearly all hospitals; in one, a dedicated ventilator was used for patients with AIDS.

There was information about the time between initiation of treatment and admission to the ICU in 18 of the cases. In only one case was the admission time greater than 7 days. This patient died. There was no discernible difference in the treatment-to-admission times between the survivors and nonsurvivors in this limited group.

Discussion

The overall mortality of 72% for patients admitted to ICUs with AIDS is similar to the figure of 77% reported in an American study.¹ The most common indication for admission in the present study was respiratory failure; PCP was the presumed causative organism in all but one case, although cytomegalovirus was present in seven. The mortality in patients with PCP who required artificial ventilation was 84%; in the American study, the mortality was 91% in a similar group of patients.¹ In the majority of patients with PCP or cytomegalovirus, the diagnosis was confirmed microbiologically. This implies that bronchoscopy was probably used to identify the causative organism. Bronchoscopy may have a sensitivity of up to 85%² if bronchial biopsy is included, and its use in the early diagnosis of these problems is becoming more frequent.³

The data relating to the duration of the period between initiation of treatment and admission to the ICU were incomplete and no conclusions can be drawn. The intention behind this search for information was to identify whether early identification and treatment of serious complications in patients with AIDS resulted in a more favourable outcome. This may be an area for further evaluation.

In this study all the patients admitted to the ICU were nursed in isolation cubicles. Only one of the intensive care units used a dedicated ventilator for patients with AIDS. This is a controversial area but there is no doubt that such a policy would pose serious problems for many units in terms of availability of resources.

It is interesting to note that antibody testing was positive in all the cases reported. Clear guidelines have not been delineated in respect of antibody screening of patients admitted to ICUs. Where close nursing and medical management of the patient are necessary, there is an argument for knowing the antibody status.

In conclusion, this survey showed a small but significant survival in a group of AIDS patients treated in ICUs. The survivors, whose average age was 37 years, were discharged home following treatment although their long-term prognosis was poor. However, patients with AIDS who present to ICU with respiratory failure have overall an extremely poor prognosis (72% mortality). In the past year there have been no definite major therapeutic advances to alter this prognosis, although this may change in the future. For example, if the initial promising results with azidothymidine are confirmed, then this will provide a further stimulus to the aggressive treatment of patients with AIDS who present with severe pulmonary disease.

Awareness of the limitations of ICUs may result in a more critical selection of patients who may benefit from their facilities. It is possible that the cases reported so far, may include some in whom intensive care was offered only at a very late stage in their respiratory failure and that the outlook might have been better with earlier intervention. Another aspect to consider is that the patients themselves, who know more about the disease process and the limitations of intensive care, may decline the rigours of ICU admission in the terminal stages of their disease. Continual re-evaluation of the role of ICUs is necessary, especially if new therapeutic measures are developed.

Acknowledgments

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References

1. SCHEIN RMH, FISCHL MA, PITCHENIK AE, SPRUNG CL. ICU survival of patients with acquired immunodeficiency syndrome. *Critical Care Medicine* 1986; 14: 1026-7.
2. COLEMAN DL, DODEK PM, LUCE JM, GOLDEN JA, MURRAY JF. Pneumocystis pneumonia and other opportunistic lung infections in patients with acquired immunodeficiency syndrome: utility of fiberoptic bronchoscope. *American Review of Respiratory Disease* 1983; 127: 81A.
3. POZNIAK AL, SWINBURN CR, JOHNSON N. Management of AIDS pneumonia. *British Journal of Diseases of the Chest* 1985; 79: 105-14.

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Reducing the risks of laryngoscopy in anaesthetised infants

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Summary

We have evaluated the use of oxygen insufflation during laryngoscopy with an Oxyscope™ laryngoscope blade compared to conventional laryngoscopy for maintenance of transcutaneous PO₂ during intubation of anaesthetised, spontaneously breathing infants. Twenty healthy children aged between 1 and 24 months were anaesthetised with halothane in oxygen. Laryngoscopy and intubation were performed in a double-blind fashion using a Miller No. 1 Oxyscope™ blade either with or without oxygen

insufflation. Transcutaneous oxygen tension, arterial pressure and heart rate were measured before and after laryngoscopy, and duration of laryngoscopy was recorded. Transcutaneous oxygen tension decreased by 7.1% (SD 6.1%) when oxygen insufflation was used, compared to 33.0% (SD 15.1%) without oxygen insufflation ($p < 0.0001$). There were no significant differences in mean duration of laryngoscopy or patient age. We conclude that oxygen insufflation during laryngoscopy and intubation of spontaneously breathing, anaesthetised infants effectively minimises the decrease in transcutaneous oxygen tension from pre-laryngoscopy levels, and makes instrumentation of the airway safer.

Key words

Anaesthesia; paediatric.

Intubation, tracheal; laryngoscopy, oxygen insufflation.

Laryngoscopy and tracheal intubation are techniques which are performed routinely by the anaesthetist to secure the airway for general anaesthesia. A decrease in arterial partial pressure of oxygen (P_{aO_2}) during the period of laryngoscopy is a common and expected occurrence during this procedure. This happens particularly in children because of their increased oxygen utilisation, smaller functional residual capacity and greater cardiac output.¹ In addition, anatomical differences in their airways as compared to adults (relatively large tongue and small oropharynx; more cephalad position of the larynx; and long, curved, more posteriorly directed epiglottis)² often result in challenges during laryngoscopy and intubation. Hypoxaemia, especially in combination with vagal stimulation produced by laryngoscopy itself, can lead to bradycardia, premature ventricular contractions and, ultimately, cardiovascular collapse.³ We have studied the efficacy of oxygen insufflation during laryngoscopy via a Miller No. 1 Oxyscope™ blade compared to laryngoscopy without oxygen insufflation for maintenance of transcutaneous oxygen tension (P_{tCO_2}) during tracheal intubation in children.

Methods

The study was approved by the Institutional Review Board of the University of Texas Health Science Center and informed consent was obtained from the parents. We studied 20 healthy children (aged between 1 and 24 months) who required general anaesthesia with tracheal intubation for elective surgical procedures. Patients were excluded if cardiorespiratory dysfunction, infection or acid-base imbalance was present or if pre-existing airway abnormalities resulted in stridor, tachypnoea or expected difficulties in airway management. The patients were assigned randomly in a double-blind fashion to one of two groups: those to undergo laryngoscopy with oxygen insufflation (group A), and those to undergo laryngoscopy in the usual fashion without oxygen insufflation (group B).

A precordial stethoscope, electrocardiograph, automatic blood pressure cuff and transcutaneous oxygen monitor (Trans-send, Sensor Medics) were attached in the operating room. The patient was then anaesthetised with halothane in oxygen and spontaneous ventilation was maintained. An intravenous infusion was started and glycopyrronium 0.01 mg/kg administered to reduce the risk of bradycardia during intubation. A satisfactory depth of anaesthesia prior to laryngoscopy was confirmed by small, midline pupils, loss of eyelid reflex, and the presence of shallow but regular respirations. No muscle relaxants were given. The anaesthetist performed laryngoscopy when P_{tCO_2} had stabilised for 60–90 seconds, using a Miller No. 1 Oxyscope™ blade either with oxygen insufflation at 4 litres/minute or without supplemental oxygen (depending on the patient's assigned group), and the trachea was intubated. Each laryngoscopy was carried out by an anaesthetist in training under the direct supervision of one or more of the investigators. The duration of each laryngoscopy was recorded (measured from the time the laryn-

goscope blade passed the lips, to the time at which the system was connected to the properly positioned tracheal tube); this period was not allowed to continue for longer than 45 seconds. P_{tCO_2} , arterial pressure and heart rate were recorded both before and after laryngoscopy. The remainder of the anaesthetic was administered in the usual fashion as dictated by the surgical procedure.

The data were analysed using a one-way analysis of variance in order to calculate the 95% confidence intervals and to test for significance. The significance level was set at 0.05.

Results

The mean (SD) percentage decrease in P_{tCO_2} was 33.0% (15.1) in group B but 7.1% (6.1) in group A ($p < 0.0001$). There was no significant difference between the two groups with regard to either patient age or duration of laryngoscopy. The mean pre-laryngoscopy P_{tCO_2} value was slightly lower in group B but this difference was not significant.

Discussion

Protection of the patient against hypoxaemia during airway manipulation and intubation is the goal of every anaesthetist. Traditionally, measures to prevent hypoxaemia have included pre-oxygenation with nitrogen washout, and the maintenance of spontaneous ventilation in the patient during the act of laryngoscopy. However, it was recently shown in healthy neonates who underwent awake intubation,⁴ and it is our clinical impression in anaesthetised children, that these measures alone do not always preclude hypoxaemia and its consequences.

Wung *et al.*⁵ demonstrated a method by which P_{aO_2} could be maintained in a neonate with bronchopulmonary dysplasia during awake nasotracheal intubation. They insufflated oxygen via a suction catheter taped to the laryngoscope blade and measured P_{tCO_2} . More recently, a modified laryngoscope blade (Oxyscope, Puritan-Bennet Corp., Foregger Medical Division, Langhorne, PA) was developed and used to prevent hypoxaemia during awake laryngoscopy and intubation in healthy neonates⁴ and in those with hyaline membrane disease.⁶ Because of these findings, oxygen insufflation during laryngoscopy is now widely accepted as an effective means of making awake laryngoscopy safer, especially in seriously ill children.

The authors recognise that this technique is probably not necessary in the routine intubation by experienced laryngoscopists of healthy infants with normal airways. We do consider, however, that it can increase the margin of safety when an airway is to be established under circumstances where relatively prolonged laryngoscopy is anticipated. For instance, we have shown this method to be useful at our training institution where the mean duration of laryngoscopy for our 20 patients was about 28 seconds, somewhat longer than a more experienced laryngoscopist would be expected to require for tracheal intubation in a child. No

Table 1. Changes in transcutaneous oxygen tension with and without oxygen insufflation.

Patient number	Age (months)	Transcutaneous oxygen tension (kPa)			Duration of laryngoscopy (seconds)
		Before laryngoscopy	At conclusion of laryngoscopy	Change (%)	
<i>Group A (oxygen insufflation at 4 litres/minute)</i>					
1	2	21.9	21.2	-2.9	40
2	24	23.1	21.6	-14.9	27
3	2	18.7	18.8	+3.7	16
4	14	38.2	32.6	-14.6	41
5	17	16.4	11.7	-6.4	35
6	6	15.8	14.4	-9.2	30
7	24	20.2	18.9	-6.6	25
8	13	27.1	27.3	+0.5	18
9	14	36.0	32.5	-10.0	21
10	8	29.7	26.3	-11.2	32
Mean (SD)	12.4 (8.0)	26.3 (9.4)	24.2* (7.7)	-7.1** (6.1)	29 (9)
95% confidence intervals		(19.6-33.0)	(18.7-29.6)		
<i>Group B (no oxygen insufflation)</i>					
1	16	18.1	13.3	-26.5	37
2	13	12.1	8.7	-28.6	14
3	9	31.4	23.9	-23.7	18
4	5	24.3	17.8	-26.8	26
5	23	30.6	18.9	-38.3	30
6	8	32.2	22.6	-29.8	14
7	24	20.1	12.5	-37.8	45
8	3	27.3	22.0	-19.5	28
9	5	14.5	10.6	-26.6	24
10	10	22.5	6.2	-72.8	41
Mean (SD)	11.6 (7.4)	23.3 (7.1)	15.6* (6.3)	-33.0** (15.1)	28 (11)
95% confidence intervals		(18.2-28.4)	(11.2-20.1)		

* $p = 0.014$; ** $p < 0.0001$.

Ptco₂ value decreased to a hypoxaemic level, with the possible exception of one patient, but oxygen insufflation clearly prevented decreases to anywhere near a potentially dangerous range during laryngoscopy. However, had laryngoscopy been longer, or the intubation unsuccessful, patients who underwent laryngoscopy without supplemental oxygen would probably have developed arterial desaturation sooner than those in whom oxygen was insufflated.

The situation which occasionally faces most anaesthetists, and which might represent the most important application of this technique, is the child with an airway abnormality (such as Treacher-Collins syndrome, the Pierre Robin anomaly, or the child with cystic hygroma)⁷ who presents for a general anaesthetic. Laryngoscopy for this group of patients is often prolonged and repeated attempts at intubation may be necessary in order to establish an airway. Hypoxaemia may be prevented, or at least its development delayed, in these patients if a high fractional concentration of inspired oxygen is delivered. This may also provide the laryngoscopist with additional time to establish the airway.

Our reliance upon transcutaneous rather than actual arterial values for partial pressure of oxygen represents a minor but necessary compromise in our protocol. We could not justify the invasiveness of arterial puncture in otherwise healthy children and it would be difficult to sample at an appropriate time to discover the lowest Pao₂ values. Ptco₂ readings correlate well with Pao₂ values in neonates throughout a wide range of oxygen partial pressure.⁸

In conclusion, the authors support the use of oxygen

insufflation via the Oxyscope™ laryngoscope blade during management of the infant airway. We consider that this technique is potentially very useful in the operating room, particularly at training institutions where a less experienced laryngoscopist may require more time to carry out tracheal intubation. The technique may be useful also in maintaining adequate oxygenation during difficult and sometimes prolonged attempts at intubation of children with an anatomical abnormality of the airway.

References

1. DRIPPS RD, ECKENHOFF JE, VANDAM LD. *Introduction to anesthesia*. Philadelphia, PA: W. B. Saunders Co., 1982.
2. ECKENHOFF JE. Some anatomic considerations of the infant larynx influencing endotracheal anesthesia. *Anesthesiology* 1951; 12: 401-10.
3. JACOBY J, ZIEGLER C, HAMELBERG W., MOGG A, KLASSEN K, FLORY F. Cardiac arrhythmia: effect of vagal stimulation and hypoxia. *Anesthesiology* 1955; 16: 1004-8.
4. HINKLE AJ. Laryngoscopy in the awake neonate, making it safer. *Anesthesiology Review* 1986; 13: 43-6.
5. WUNG JT, STARK RI, INDYK L, DRISCOLL JM. Oxygen supplement during endotracheal intubation of the infant. *Pediatrics* 1977; 59 (Suppl. 6): 1046-8.
6. TODRES ID, CRONE RK. Experience with a modified laryngoscope in sick infants. *Critical Care Medicine* 1981; 9: 544-5.
7. BERRY FA. *Anesthetic management of difficult and routine pediatric patients*. New York: Churchill-Livingstone, 1986.
8. HUCH R, LUBBERS DW, HUCH A. Reliability of transcutaneous monitoring of arterial Po₂ in newborn infants. *Archives of Diseases in Childhood* 1974; 49: 213-8.

Cannulation of the epidural space

A comparison of 18- and 16-gauge needles

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Summary

A group of 685 obstetric patients were randomly allocated to have their epidural block performed using either a 16-gauge or an 18-gauge Tuohy needle. Bleeding was noted from needle or catheter trauma in 18% of patients and it proved impossible to insert the catheter in 3%. The majority of mothers experienced little discomfort during the procedure but 2% found insertion to be very uncomfortable. There was no significant difference in the complication rate, ease of use, or patient discomfort between the 18- or 16-gauge needles. Epidural analgesia, although safe, is not without hazard. It may be difficult to perform and may, rarely, cause considerable discomfort.

Key words

Anaesthetic techniques, regional; epidural. Complications.

Tuohy needles were originally developed for continuous subarachnoid anaesthesia¹ but were quickly adapted for the passage of catheters into the epidural space.² The techniques and equipment used have been modified continuously since then^{3–6} and, with improvements in manufacturing techniques, 18-gauge needle-catheter assemblies have become available which allow the easy passage of a catheter sufficiently large to permit the injection of local anaesthetic with acceptable ease. It is believed that small diameter needles minimise trauma to the tissues and the size of dural tear, should dural puncture occur.

The aim of this study was to determine if there was any difference between 16- and 18-gauge needles in their respective complication rates, ease of use and patient discomfort. No attempt was made to record complications that related to the block itself (hypotension, total spinal, etc.) since these have been well documented in previous studies.^{6–8}

Methods

A total of 685 mothers who had elected to receive epidural analgesia in labour were randomly allocated to have their block administered with a 16- or 18-gauge Tuohy needle and catheter system (Portex Minipack). The block was performed using the midline approach and the loss of resistance technique. The position of the patient during the procedure was that preferred by the anaesthetist; the majority of blocks were performed in the sitting position.

A questionnaire which recorded the following information was filled out on completion of the procedure: dural puncture by needle; bleeding following needle insertion (bloody tap); dural puncture by catheter; entry of vein by catheter (blood freely aspirated from catheter); bleeding caused by catheter (blood in catheter but unable to aspirate); catheter difficult to insert but eventually passed; catheter impossible to insert; catheter resited for any of the above reasons.

The anaesthetist who performed the block then assessed the ease with which cannulation was achieved by marking a 10-cm visual analogue score. Three hundred and eighteen of the mothers were asked to indicate the discomfort they experienced by a similar visual analogue score.

The results were analysed by the Chi-squared method. A *p* value < 0.05 was considered to indicate a significant difference.

Results

The results are summarised in Table 1. Twenty-five percent of epidurals had one or more of the listed complications recorded. Four dural punctures occurred; three were associated with the use of 18-gauge needles and one occurred with a catheter passed through a 16-gauge needle, a difference which is not statistically significant.

Twelve percent of epidural catheters were considered difficult to insert, while 3.5% were impossible to insert and had to be resited. Six percent had to be resited for other reasons, such as bleeding. Eighteen percent of procedures were associated with evidence of bleeding.

The overall complication rate, the incidence of each individual complication and the distribution of pain scores were similar for both sizes of needle. Any differences which did exist did not reach statistical significance.

Discussion

It has been suggested that the finest gauge epidural needles should be used to minimise tissue trauma and reduce the severity of headache should dural puncture occur.⁹ Conversely, it can be argued that the larger size of needle is more rigid and gives a better 'feel' as it passes through the ligaments, and is less sharp and less likely to puncture the dura. Clearly, the anaesthetist who administered the block in this study was aware of the needle size used and, to this extent, the opinion of ease of use is influenced by the beliefs or prejudices of that individual. However, the incidences of bleeding, resiting, dural puncture, etc., are objective observations.

This study failed to detect any difference in the complication rate for the two sizes of needle. The number of dural punctures was greater with 18-gauge needles but the difference was not statistically significant. The total number of epidurals which had to be resited, for whatever reason, was surprisingly high, 10% for both sizes of needle. It is

Table 1. Results of epidural study.

	16-gauge needle (n = 334)		18-gauge needle (n = 351)		Total	(%)
	Number	(%)	Number	(%)		
Dural puncture (needle)	0	(0.0)	3	(0.85)	3	(0.44)
Bloody tap (needle)	12	(3.6)	7	(1.99)	19	(2.77)
Dural puncture (catheter)	1	(0.3)	0	(0.0)	1	(0.15)
Caused bleeding (catheter)	25	(7.49)	25	(7.12)	50	(7.30)
Entered vein (catheter)	28	(8.38)	27	(7.69)	55	(8.03)
Difficult to insert catheter	38	(11.4)	49	(14.0)	87	(12.70)
Impossible to insert catheter	9	(2.69)	15	(4.27)	24	(3.50)
Resited	35	(10.5)	35	(10.0)	70	(10.2)
Total	81	(24.2)	90	(25.6)	171	(25)
<i>Pain on insertion</i>	(n = 168)		(n = 150)		(n = 318)	
Mean pain score	1.7		1.75		1.72	
Pain score >7	3		3		6	
	(1.8%)		(2%)		(2%)	
Pain score <3	135		117		252	
	(80%)		(78%)		(79%)	

also interesting to note that either a complication or a technical difficulty arose in a quarter of all procedures.

Eighteen percent of epidurals (in both groups) were associated with some evidence of bleeding, although in the majority the bleeding was slight. This incidence is higher than that reported by Dawkins¹⁰ and Verniquet,¹¹ and confirms the danger of inserting epidurals in patients with a coagulopathy. No instructions were given about the use of an injection of fluid via the needle before the catheter was inserted, although this has been shown to reduce the incidence of vessel puncture by the catheter.¹¹

The pain experienced on insertion of spinal needles has been shown to be proportional to the size of the needle used.¹² Our findings show that there was no difference in the discomfort caused by the two needles, once the skin was infiltrated with local anaesthetic. It is also important to recognise that a small number of patients (2%) experience severe discomfort (pain score > 7.0).

Epidural analgesia is unquestionably the most effective form of pain relief and should be made available to all mothers in labour. However, its inception may, rarely, be very painful. Difficulties in insertion and minor complication are relatively common as this study indicates. Both the immediate and long-term effects of these complications are insignificant for the vast majority but they are a cause for concern at the time of insertion of the epidural needle and cannula. Care is needed during insertion of the catheter, with meticulous supervision and monitoring following the initial injections of local anaesthetic through the catheter. The relatively high incidence of epidural bleeding suggests that epidural analgesia should not be administered to patients with a coagulation disorder or those who are receiving anticoagulants.

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References

1. TUOHY EB. Continuous spinal anesthesia: a new method utilizing a ureteral catheter. *Surgical Clinics of North America* 1945; **25**: 834-40.
2. CURBELO MM. Continuous peridural segmental anesthesia by means of a ureteral catheter. *Anesthesia and Analgesia* 1949; **28**: 13-33.
3. LEE JA. Specially marked needle to facilitate extradural block. *Anaesthesia* 1960; **15**: 186.
4. LEE JA. A new catheter for continuous extradural analgesia. *Anaesthesia* 1962; **17**: 248-50.
5. DOUGHTY A. A precise method of cannulating the lumbar epidural space. *Anaesthesia* 1974; **29**: 63-5.
6. BROMAGE PR. *Epidural analgesia*. London: W. B. Saunders, 1978.
7. CRAWFORD JS. Some maternal complications of epidural analgesia for labour. *Anaesthesia* 1985; **40**: 1219-25.
8. DOUGHTY A. Lumbar epidural analgesia—the pursuit of perfection. With special reference to midwife participation. *Anaesthesia* 1975; **30**: 741-51.
9. PAULL J. Rational choice of single shot or catheter techniques in epidural analgesia. In: *WFSA lectures, Vol. 1*. Oxford: Blackwell Scientific Publications, 1984: 1-8.
10. MASSEY DAWKINS CJ. An analysis of the complications of extradural and caudal block. *Anaesthesia* 1969; **24**: 554-63.
11. VERNIQUET AJW. Vessel puncture with epidural catheters. Experience in obstetric patients. *Anaesthesia* 1980; **35**: 600-2.
12. DANIELS M, PARK GR. Is a local anaesthetic necessary when using fine gauge spinal needles? *British Medical Journal* 1985; **290**: 820-1.

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Pulmonary haemorrhage as a complication of neonatal anaesthesia

This is a report of a neonate in whom respiratory collapse and pulmonary haemorrhage occurred after induction of anaesthesia with thiopentone and atracurium, and we speculate that drug precipitation led to pulmonary micro-emboli.

He was the first child of healthy, unrelated English parents, born at term after a normal pregnancy and delivery, and weighed 2.67 kg at birth. He was admitted at 19 days with a 3-day history of a groin swelling on the right. He had one loose stool and one vomit on the day of

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admission. Examination revealed a vigorous infant with a reducible right inguinal hernia. He fed well and had no further vomiting or loose stools after admission. It was decided to repair his hernia prior to discharge.

Anaesthesia was induced intravenously after pre-oxygenation, with thiopentone 4 mg/kg (10 mg) followed by atracurium 0.4 mg/kg (1 mg) into a running infusion. Cyanosis developed immediately and persisted despite tracheal intubation and controlled ventilation of his lungs with 100% oxygen, although the pulse rate and cardiac output remained good; the lowest recorded pulse rate was 101 beats/minute. The tracheal tube was changed with little improvement; at this stage blood stained froth was aspirated from the tube, although there was no obvious trauma or oedema. Cyanosis persisted for a further 20 minutes. The operation was abandoned and the atracurium reversed with neostigmine 0.1 mg, after 0.15 mg atropine given earlier.

The baby initially remained pink with good respiratory effort in 35% oxygen after extubation but became cyanosed and unresponsive after 30 minutes. The trachea was reintubated and again no traumatic lesion was seen but frank blood was aspirated from the tracheal tube, with a decrease in haemoglobin from 12 to 9 g/dl. High peak inspiratory pressures (maximum 5.0 kPa) were required over the next 12 hours; he was severely acidotic (lowest pH 6.6), hypoxic (P_{aO_2} 3.6 kPa) and hypotensive (blood pressure 30 mmHg systolic). He received intravenous bicarbonate and inotropic support. The chest X ray showed a normal heart shadow with bilateral diffusely increased pulmonary shadowing which rapidly increased to a bilateral 'white-out'. The ECG showed changes of right ventricular strain which subsequently returned to normal. Echocardiogram and clotting studies were normal. He required controlled ventilation for 10 days; vecuronium was used to maintain neuromuscular blockade. There was gradual resolution of the chest X ray opacity and a decreased requirement for additional oxygen.

He underwent an uneventful herniotomy and orchidopexy on the 10th day of ventilation after gaseous induction with isoflurane and muscle paralysis with vecuronium. He was within normal developmental limits when reviewed at the age of 3 months. ECG and chest X ray returned to normal within 4 weeks of his initial collapse.

Four possible mechanisms are suggested for his collapse.

Aspiration of acid stomach contents. He was noted to be 'chesty' after feeds during his convalescence. Barium swallow showed marked gastro-oesophageal reflux and his

feeds were subsequently thickened, with resolution of these symptoms. His presenting illness may have been of significance in this possibility. However, no gastric contents were evident in his pharynx or trachea and massive pulmonary haemorrhage is not a feature of Mendelson's syndrome.

A local vascular lesion in a main bronchus. No obvious bleeding lesion was seen on any of several laryngoscopies and subsequent high kilovoltage views of the trachea and main bronchi revealed no abnormality.

Severe allergic reaction to anaesthetic agents. There have been several reports of anaphylactoid reactions to induction agents and muscle relaxants.¹⁻³ These are mediated via circulating immunoglobulins, activation of complement by the classical or alternate pathways and by the pharmacological release of histamine.⁴ No evidence of an immune abnormality was found. Complement profiles and immunoglobulin levels were normal. The patient's basophils showed a normal histamine response to anti-IgE but no increase in histamine release compared to control when subjected to both standard and 10 times standard concentrations of atracurium *in vitro*. Similar responses were obtained with vecuronium.

Precipitation of atracurium and thiopentone. It is known that these agents precipitate when mixed in solution. The drugs were given separately into a running infusion but it is possible that drug micro-aggregates may have caused widespread pulmonary embolism and acute pulmonary hypertension.

This is to our knowledge the first reported case of pulmonary haemorrhage in association with these anaesthetic agents. We have reported this patient to the Committee on Safety of Medicines as a case of adverse reaction to anaesthesia which involved atracurium and thiopentone.

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References

1. POLLOCK EMM, MACLEOD AD, McNICOL LR. Anaphylactoid reaction complicating neonatal anaesthesia. *Anaesthesia* 1986; 41: 178-80.
2. WOODS I, MORRIS P, MEAKIN G. Severe bronchospasm following the use of atracurium in children. *Anaesthesia* 1985; 40: 207-8.
3. Committee on Safety of Medicines. *Current problems* 14. 1985.
4. WATKINS J. Anaphylactoid reactions to i.v. substances. *British Journal of Anaesthesia* 1979; 51: 51-60.

Bradycardia during neurosurgery—a new reflex?

Bradycardia during neurosurgical procedures under general anaesthesia is not uncommon and may be related to several causes.¹ A case is reported where basic anatomical knowledge led to an understanding of one such cause which has not been reported previously in the anaesthetic literature.

A 34-year-old, 60-kg woman was scheduled to undergo left temporal lobectomy for uncontrolled temporal lobe seizures. There was no other significant medical history. Current medication was carbamazepine 800 mg daily. Physical examination was normal and the electrocardiogram showed sinus rhythm of 70 beats/minute.

Premedication was with oral diazepam 10 mg 2 hours before induction with fentanyl 120 µg droperidol 1 mg and thiopentone 300 mg. Relaxation for tracheal intubation was with atracurium 40 mg. Anaesthesia was maintained with 30% oxygen in nitrous oxide with the addition of 0.5% isoflurane and controlled ventilation of the lungs; the fresh

gas flow was adjusted to maintain end tidal PCO_2 at 4 kPa. Muscle relaxation was maintained with a continuous infusion of atracurium 5 mg/ml in 0.9% saline given via a syringe driver at a rate sufficient to maintain a post-tetanic count of less than 5 as assessed by a peripheral nerve stimulator.

Anaesthesia was uneventful during craniotomy and temporal lobectomy; the heart rate was stable (60-70 beats/minute) and the systolic blood pressure 110 mmHg. A severe sinus bradycardia of less than 20 beats/minute occurred when the surgeon assessed haemostasis, with hypotension to 80 mmHg systolic. End tidal PCO_2 did not alter. The surgeon stated that he was using the diathermy in the region of the tentorium with no undue retraction on any structure. The heart rate gradually returned to its previous level when this was stopped. A small bleeding point near the junction of the tentorium cerebelli with the floor of the

middle fossa required further diathermy but the patient's heart rate again decreased as soon as the bipolar diathermy was activated, this time with complete atrioventricular dissociation which progressed rapidly to transient asystole. Cessation of diathermy once again allowed the heart to regain sinus rhythm with a rate of 60 beats/minute. It could be shown that physical application of the diathermy forceps did not cause this effect but a severe bradycardia resulted as soon as the diathermy current was on. This was disconcerting because the vessel continued to bleed. Consideration of applied anatomy gave a possible explanation for this effect which had not been seen by the surgeon before, and the heart rate increased to 100 beats/minute after administration of 0.6 mg atropine intravenously but did not slow below 80 beats/minute when the diathermy was reapplied and the vessel sealed. The remainder of the procedure, reversal and recovery were uneventful.

This episode can be explained as a neurosurgical version of the oculocardiac reflex.² The afferent part of that reflex is through the ciliary nerves and the ophthalmic division of the trigeminal nerve to the spinal tract of the trigeminal. This is close to fibres from the cardioinhibitory centre (nucleus ambiguus) which pass to the vagus as the efferent limb of the reflex, to cause severe bradycardia.³ The diathermy stimulation was applied to the dura mater which forms the lining of the middle cranial fossa and the tentorium cerebelli. The sensory nerve supply of this region is from recurrent tentorial branches of the

ophthalmic nerve⁴ and these nerves could constitute the afferent limb of a meningocardiac reflex in the same way as stimulation of the ciliary branches.

Atropine has been shown to diminish the severity of the oculocardiac reflex effectively as it did in the case described. Awareness of this potential problem in neuro-anaesthesia based on the application of applied anatomy and neurology leads to a rational use of this agent when required.

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References

1. MARSHALL M. *Neuronanaesthesia. Current topics in anaesthesia*, Vol. 3. London: Edward Arnold, 1979: 22-3.
2. MOONIE GT, REES DL, ELTON D. The oculocardiac reflex during strabismus surgery. *Canadian Anaesthetists' Society Journal* 1964; 11: 621-32.
3. DEWAR KMS, WISHART HY. The oculocardiac reflex. *Proceedings of the Royal Society of Medicine* 1976; 69: 373-4.
4. ROMANES GJ. The central nervous system. In: ROMANES GJ, ed. *Cunningham's textbook of anatomy*. London: Oxford University Press, 1972: 696.
5. KERR WJ, VANCE JP. Oculocardiac reflex from the empty orbit. *Anaesthesia* 1983; 38: 883-5.

Caudals and antisepsis

Why do authors and anaesthetists treat the caudal approach to the epidural space so casually whilst they advocate more stringent rules for the lumbar approach to the same space? One chapter of a recently published textbook on regional anaesthesia¹ has two photographs separated by a single page. One shows a lumbar epidural needle inserted by a gloved and gowned anaesthetist. The other shows a caudal epidural needle inserted by ungloved hands at the end of hairy arms. One large thumb rests on the sacral cornu very near the shaft of the needle.

The author of the chapter is an expert and can obviously perform these blocks easily and quickly. However, we often see caudal blocks performed by far less accomplished anaesthetists and trainees with only minimal regard for sterility or for the proximity of the anus and perineum to the injection site. These same anaesthetists will religiously

scrub up to perform a lumbar epidural. It is incorrect to claim that infection never occurs since we recently had a patient referred to St Thomas' Hospital with a sacral abscess after caudal injection. The outcome of established sacral abscesses can be very poor.

If caudal injection were accorded a higher status (and this may include the anaesthetist wearing gloves) then these occasional tragedies might perhaps be avoided.

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References

1. WILDSMITH JAW, ARMITAGE FN. *Principles and practice of regional anaesthesia*. Edinburgh: Churchill Livingstone, 1987.

Medicolegal aspects of anaesthesia

A quarter of Professor Spence's October review of *Anaesthesia Review* 4 concerned Dr Green's chapter and ended with a condemnation of 'ex-cathedra statements of medicolegal camp followers'. He has missed the point. The courts judge negligence by 'the standard of the ordinary skilled man exercising and professing to have that special skill'.¹ Thus all of us set (and continually modify) the expected standards of practice. In this sense we are all medicolegal camp followers but we can only form our opinions from the experiences of ourselves and others.

Therein lies the value of such a chapter. The defence societies amass a large store of unique data which is otherwise unobtainable. It is merely hinted at by their annual reports and of course cannot be published in detail, at least for many years. Dr Green presented some of this information and I suspect that many anaesthetists will value it when they plan improvements in their service to patients. Instances include junior staff training and the purchase of

monitoring equipment. It might even help to control costs at a time when 1000 defence society subscriptions (those paid by half of all consultant anaesthetists in England and Wales) can be lost in a single settlement—*res ipsa loquitur*.

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References

1. BOLAM V. FREERN HOSPITAL MANAGEMENT COMMITTEE. *All England Law Reports* 1957; 2: 118-28.

A reply

Thank you for sending me the letter from Dr Davies which comments on my remarks about Dr Green's chapter in the latest of the *Anaesthesia Review* series. Dr Green has indeed

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1. Feldman SA, Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
2. Basta SA, Clinical Experiences with Norcuron, Excerpta Medica (1983) 183-184



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presented some of the information contained in the files of a defence society and I agree that such information may be of value.

My general point is that writers on such topics often go beyond the facts on which they report, to give a personal interpretation. Such interpretations that appear in chapters entitled 'Medicolegal aspects of anaesthesia' (or in publications by defence societies) seem to demand special recognition by virtue of the authority of the writer, and may receive it in medicolegal circles. Dr Green offers a list of potentially expensive monitoring equipment which he considers to be mandatory or essential. He does not offer any evidence that failure to use such equipment has been an embarrassment to a doctor who attempts to defend himself in a civil action. If it is a matter of opinion, it could be argued that such an

array (automatic sphygmomanometer, digital pulse monitor, electrocardiogram, capnometer, disconnection alarm, oxygen analyser) is ergonomically unsound and thus potentially dangerous.

Writing of that kind may bring great joy to the manufacturers of electromedical equipment but I do not think either anaesthetists or those who stand ready to defend them should regard the statements as anything other than menacing. As in the book review, may I repeat that I have no wish to pick on Dr Green specially. My comments also relate to a number of people who talk and write to us about medicolegal issues.

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A.A. SPENCE

Repair of thoracic aorta and subsequent pregnancy

Traumatic rupture of the thoracic aorta indicates a major physical insult. The strength of the aorta always remains suspect, especially during pregnancy.

A primipara admitted at 38 weeks had an aneurysmectomy of the descending aorta followed by dacron grafting 18 months before admission. She went into labour at 39 weeks. An epidural catheter was placed at the L₃-L₄ interspace and 10 ml bupivacaine 0.25% injected. She was painfree and, at 8-cm dilatation of the cervix, she was seated and 12 ml of the same solution injected. A vacuum extraction was performed when the head presented.

Aortic aneurysm is an extreme rarity at child bearing age. Caesarean section under general anaesthesia was performed in the few reported cases.¹ The reasons stated for this choice are changes in the aortic wall during pregnancy which consist of accumulation of mucoid material, a decrease in acid mucopolysaccharides in the reticulum fibres of the arterial wall, and hypertrophy of smooth muscle.^{2,3} Contractions in the first stage of labour cause an increase of 30-45% in cardiac output, blood volume increases by 300-500 ml and arterial blood pressure by 15-25%. It is known that epidural analgesia attenuates these changes.

There seems to be no reason, unless obstetrically indicated, not to allow a parturient who has had an aneurysmectomy to deliver vaginally under epidural analgesia and assisted delivery. This circumvents the increase in blood pressure, the pain and the anxiety and so prevents increased pressure in a suspect aorta.

Rupture of a previously repaired coarctation of the aorta with a dacron graft in the sixth month of pregnancy was attributed to the weakness in the arterial wall.⁴ These parturients should be supervised carefully during the antenatal period. They have to be managed by elective Caesarean section if any obstetric problem is anticipated or arises. If not, a well conducted selective epidural analgesia should be performed so as to prevent haemodynamic changes during the first stage and during assisted delivery.

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References

1. MERIN G, BITRAN D, DONCHIN Y, WEINSSTEIN D, BORMAN JB. Traumatic rupture of the thoracic aorta during pregnancy. Surgical Considerations. *Chest* 1981; **79**: 99-100.
2. MANALO-ESTRELLA P, BARKER AE. Histopathologic findings in human aortic media associated with pregnancy. A study of 16 cases. *Archives of Pathology* 1967; **83**: 336-41.
3. MANDEL W, EVANS EW, WALFORD RL. Dissecting aortic aneurysm during pregnancy. *New England Journal of Medicine* 1954; **251**: 1059-61.
4. DAVIS JE, LEIDER HJ. Rupture of prosthetic graft in pregnancy. *American Journal of Obstetrics and Gynecology* 1977; **128**: 397-9.

A new connector for use in cricothyroid puncture

Oxygenation via a wide bore intravenous cannula that has been passed through the cricothyroid membrane is a well described method for the management of patients with upper airway obstruction.¹ A 3.5-mm standard tracheal tube connector may be inserted into the hub of the cannula to connect to the 15-mm taper of a catheter mount. A 7-mm connector may be inserted into the barrel of a 2-ml syringe, or an 8-mm connector into a 3-ml syringe² which can then be attached to the cannula. Another method is to attach the barrel of a 10-ml syringe to the cannula and an 8-mm tracheal tube can then be inserted into the bevel and an air-tight fit obtained by inflation of the cuff.³ All of these connexions are bulky and increase the risk of the cannula becoming kinked or dislodged from the trachea. They are also liable to become disconnected from the cannula.

We have developed a connector to overcome these problems with a Luer-lock fitting and safety lock. A 5.5-

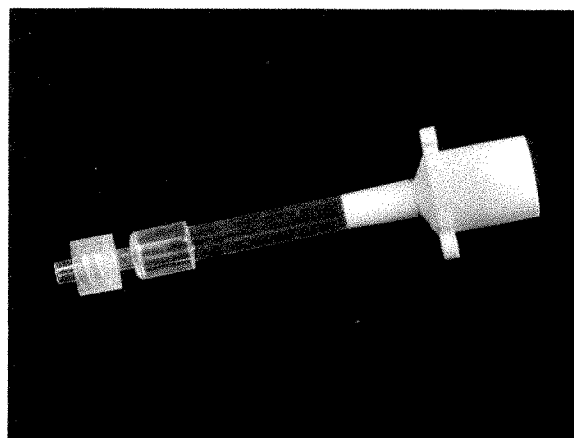


Fig. 1. A new connector for use in cricothyroid puncture.

cm piece of clear PVC tubing distances this from a standard 4-mm connector onto which the tubing is welded (Fig. 1). Condensation from expired gas can be seen in the tubing which is an added advantage. The connector is to be manufactured by Portex Ltd, Hythe, Kent.

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Single breath induction

The recent correspondence on the subject of rapid inhalational induction of anaesthesia is of particular interest since I recently completed a study of single breath induction of anaesthesia with isoflurane in 70% nitrous oxide, and some of the findings and conclusions are at variance with Dr Galloway and Drs Wilton and Thomas (*Anaesthesia* 1987; 42: 772-3).

Isoflurane was used because, in theory, it should produce a rapid single breath induction due to its low blood-gas partition coefficient, and the MAC is between that of halothane and enflurane. However, isoflurane has a very pungent odour so a 2% concentration was used in 70% nitrous oxide in order to minimise irritation to the airway.

Thirty-five patients were studied (there was a control group of 35 patients with a conventional multibreath technique) and only 19% showed any sign of movement or excitement. This compares with the findings of Drs Wilton and Thomas with halothane but is very different from the 77% of Dr Galloway, who considered that 23 out of 30 patients had breathed suboptimally; the isoflurane study had 20% in this category.

Drs Wilton and Thomas state that there was a high degree of airway irritability when they used 5% enflurane but further suggest that any lower concentration might be ineffective because of the low inspired to alveolar gradient. The isoflurane study demonstrates that there was good patient cooperation, acceptability and satisfactory induction despite a low concentration.

In summary, 2% isoflurane in 70% nitrous oxide in oxygen produced a satisfactory single breath induction of anaesthesia, is theoretically superior to enflurane and is therefore an alternative to halothane for the many occasions when the latter is unacceptable. All of these findings are soon to be published.

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J.M. LAMBERTY

A reply

Thank you for the chance to reply to Dr Lamberty's letter. Single breath isoflurane induction was recently compared to single breath halothane induction and found to be an acceptable technique.¹ The authors in this study used inspired agent concentrations approximately equal to 4.5MAC for each agent. Induction time was 38 seconds (SEM 2) for isoflurane and 86 seconds (SEM 4) for halothane. It should be noted, however, that fentanyl 5 µg/kg was given to these patients prior to inhalational induction

References

1. LATTO IP. Management of difficult intubation. In: LATTO IP, ROSEN M, Eds. *Difficulties in tracheal intubation*. Eastbourne: Bailliere Tindall, 1984.
2. STINSON TW. A simple connector for transtracheal ventilation. *Anesthesiology* 1977; 47: 232.
3. REICH DL, SCHWARTZ N. An easily assembled device for transtracheal oxygenation. *Anesthesiology* 1987; 66: 437-8.

to overcome the irritant properties of the agents by suppression of the cough reflex. Not surprisingly, all patients were intubated and ventilated. Clearly the above technique is of little value if an inhalational technique is used in short procedures in which the patient continues to breathe spontaneously.

Dr Lamberty's suggestion that 2% isoflurane produces a rapid induction that is acceptable to the patients, is extremely interesting and of obvious practical value. Given the accepted physicochemical properties of the drug it would be interesting to know at what end tidal isoflurane concentrations the loss of consciousness occurred? Studies that have used the concept of MAC-awake² suggest that loss of consciousness occurs at approximately 50-60% of accepted MAC, i.e. 0.6-0.7% isoflurane. Thus the supplementation of 2% inspired isoflurane with 70% nitrous oxide may allow rapid loss of consciousness. Studies in children which compared 2% isoflurane and halothane in 70% nitrous oxide, however, found that induction with isoflurane took 5.42 minutes (SD 2.03) and was significantly longer than halothane induction.³ Airway irritability was a problem in the isoflurane group. With children we noted a more rapid loss of consciousness than the above study but time from loss of consciousness until surgical anaesthesia seems to be considerable even when 5% isoflurane is used.

If Dr Lamberty's patients were truly anaesthetised rather than just unconscious (i.e. loss of eyelash reflex and/or no response to noxious stimuli) then this finding is truly remarkable. We eagerly await the completed report.

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References

1. LOPER K, REITAN J, BENNETT H, BENTHUYSEN J, SNOOK L. Comparison of halothane and isoflurane for rapid anesthetic induction. *Anesthesia and Analgesia* 1987; 66: 766-8.
2. STOELTING RK, LONGNECKER DE, EGER EI. Minimum alveolar concentrations in man on awakening for methoxyflurane, halothane, ether and fluroxene anesthesia. *Anesthesiology* 1970; 33: 5-9.
3. PANDIT UA, STEUDE GM, LEACH AB. Induction and recovery characteristics of isoflurane and halothane anaesthesia for short operations in children. *Anaesthesia* 1985; 40: 1226-30.

Should air-oxygen replace nitrous oxide-oxygen general anaesthesia?

This article by Moseley and others (*Anaesthesia* 1987; 42: 609-12) makes interesting reading because in this hospital air-oxygen is replacing nitrous oxide-oxygen anaesthesia.

Nitrous oxide has become a scarce and expensive commodity since the introduction of the second tier Foreign Exchange Market last year. Rather than postpone

or cancel cases we have resorted to the use of ketamine, air, oxygen and pancuronium with intermittent positive pressure ventilation of the lungs with an Ambu bag connected to an oxygen cylinder in selected patients for major surgical procedures.

The technique consists of premedication with diazepam

and atropine, induction with hetamine 2 mg/kg, tracheal intubation after suxamethonium and maintenance with pancuronium and intermittent ketamine. The first incremental dose of ketamine is given soon after tracheal intubation in order to prevent the return of consciousness.

We have yet to examine the effects of this method on blood gases and awareness. However, one patient reported that she felt as if she was being pumped during surgery!

University of Calabar Teaching Hospital, S.G. AKPAN
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A reply

Thank you for allowing us to reply. There was no evidence of awareness during surgery in the patients we studied but we used volatile anaesthetic agents to supply anaesthesia. If nitrous oxide is scarce and expensive, the initial investment in a source of compressed air and low flow blender is worthwhile because the traditional anaesthetic machine can then be used to deliver volatile anaesthetic agents.

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Suxamethonium and myasthenia gravis

The study by Drs Wainwright and Broderick (*Anaesthesia* 1987; **42**: 950-7) reported results from five myasthenic patients given 1 mg/kg and five given 0.5 mg/kg suxamethonium which seem small numbers with which to fulfill the stated claim of 'ascertaining the incidence of a non-depolarising type of block in a series of patients undergoing thymectomy.'

The small sample size seems to have been responsible for the lack of statistical significance between some of the results, for example, the mean onset times (55.6 and 81.2 seconds in the myasthenic patients who received the same dose); this is an increase of almost 50%. Myasthenic patients who received suxamethonium 0.5 mg/kg depolarised as rapidly and had a higher incidence of non-depolarising block from which they took longer to recover as similar patients who received 1 mg/kg.

Results about depolarising block were difficult to interpret because *onset time* was not defined and the similarity between that and *circulation time* was confusing. The reader was left in some doubt as to why these two strikingly similar terms should have such widely differing reported values.

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A reply

Thank you for the opportunity to reply to the points raised by Dr Richardson. We found a much higher incidence of non-depolarising block in myasthenics who received both 1.0 and 0.5 mg/kg suxamethonium when compared to the controls. This has been reported after 1.0 mg/kg suxamethonium.¹ However, we were unable to ascertain any prediction of the incidence of non-depolarising block in terms of disease severity or dose of suxamethonium, probably due to the variation in both symptomatology and treatment in the 10 myasthenics we studied. We would

welcome further studies but the numbers involved would have to be many times greater to be assured that this aim was fulfilled. The incidence of non-depolarising block was higher in the group of myasthenics given 1 mg/kg and developed in all of the patients but in only two who received 0.5 mg/kg, not *vice versa* as is suggested by Dr Richardson.

We were unable to compare the onset time of depolarising block in the two myasthenic groups since only two patients in the 0.5 mg/kg group developed a depolarising block, the remainder were all resistant.

The onset time of depolarising block was taken as the time from injection to the reduction in T_1 to < 5% of control, which is considered to be the time to optimal intubation conditions.² Circulation time, from injection to first discernible depression of T_1 , was also measured to determine that the difference in the onset of depolarising block³ when myasthenics were compared with controls, was not due to any difference in cardiac output between the two groups but solely to an effect at the neuromuscular junction.

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References

1. AZAR I. The response of patient with neuromuscular disorders to muscle relaxants: a review. *Anesthesiology* 1984; **61**: 1973-87.
2. HARRISON GA, JUNIUS F. The effect of circulation time on the neuromuscular action of suxamethonium. *Anaesthesia and Intensive Care* 1972; **1**: 33-40.
3. MINSAS B, STOVNER J. Artery-to-muscle onset time for neuromuscular blocking drugs. *British Journal of Anaesthesia* 1980; **52**: 403-7.

McArdle's disease and Caesarean section

A 31-year-old patient with McArdle's disease, recently presented to this hospital in the 30th week of her second pregnancy. She was scheduled for delivery by Caesarean section under epidural anaesthesia. She had an emergency Caesarean section for premature labour under general anaesthesia 5 years previously. The management of the procedure was subsequently discussed in *Anaesthesia*.¹

McArdle's disease is a hereditary myopathy due to a deficiency of phosphorylase which results in failure to convert glycogen to lactate during anaerobic exercise. The principal symptom of the disease is severe and sustained

skeletal muscle cramps on strenuous exercise. About two-thirds of patients have occasional episodes of myoglobinuria, usually after severe exercise. Rarely acute renal failure has supervened.² The use of suxamethonium is contraindicated on theoretical grounds since muscle cramps may be produced by fasciculation.

Epidural anaesthesia to T₄ bilaterally was induced with 0.5% bupivacaine with 1:400 000 adrenaline, via a catheter introduced at the L₂-L₃ inter-space. A preload of one litre 0.9% saline was given and cardiovascular stability maintained throughout. An intravenous infusion of 0.18% saline

in 4% dextrose was used peri- and postoperatively, to ensure the provision of glucose as substrate for muscle metabolism.

The procedure was uneventful apart from cramp-like symptoms in the left forearm. This was probably due to the cuff of the automatic blood pressure recorder, which was set to cycle at 3-minute intervals. The use of tourniquets is not recommended³ and automatic blood pressure recording devices should be employed with caution.

Postoperative analgesia was provided by continuous epidural infusion of 0.125% bupivacaine plain for 24 hours. Subsequent analgesia on return to the ward was provided by oral paracetamol.

We conclude that regional anaesthesia rather than general anaesthesia is preferable for Caesarean section in this rare condition. However, care must be taken over the

management of intravenous fluid replacement and blood pressure measurement.

The patient and child remained well and were discharged from hospital one week after delivery.

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References

1. COLEMAN P. McArdle's disease: problems of anaesthetic management for Caesarean section. *Anaesthesia* 1984; **39**: 784-7.
2. McARDLE B. Myopathy due to a defect in muscle glycogen breakdown. *Clinical Science* 1951; **10**: 13-33.
3. FIELD RA. The glycogenoses: von Gierke's disease, acid maltase deficiency, and liver glycogen phosphorylase deficiency. *American Journal of Clinical Pathology* 1968; **50**: 20-8.

Hypothermia and the action of neuromuscular blocking agents

We would like to comment on the report by Denny and Kneeshaw (*Anaesthesia* 1986; **41**: 919-22) which indicated that the effectiveness of non-depolarising neuromuscular blocking drugs is increased during hypothermic cardiopulmonary bypass (CPB). Their conclusion that hypothermia increases neuromuscular blockade contrasts with our findings¹ that hypothermia decreases the potency of several non-depolarising neuromuscular blocking agents *in vitro*. We suggest that their report inadequately distinguished pharmacodynamic and pharmacokinetic factors. We wish to call attention to other factors in addition to temperature which may affect muscle relaxant potency during CPB, namely, changes in the volumes of distribution and redistribution.

We have occasionally noted a sudden decrease in relaxant effectiveness within 0.5-3 minutes from the start of CPB when bolus doses of vecuronium or atracurium are used to control muscle relaxation before CPB is instituted. This decreased effectiveness is manifest by diaphragm and/or patient movement, and calls for an additional small bolus of muscle relaxant to maintain control. Others have also noted an increase in relaxant requirement at the institution of CPB.² We attribute this effect, which occurs before the patient is cooled, to the infusion through the aortic canula of drug-free pump prime. We suspect that the muscle relaxant diffuses out of the neuromuscular junction, down

its concentration gradient. However, the pharmacokinetics are complex, since it has been shown that plasma muscle relaxant concentration can sometimes even increase during CPB.³ How pharmacokinetic factors affected the results of Denny and Kneeshaw, we of course do not know. However, other clinicians should keep these factors in mind as they relate Denny and Kneeshaw's findings to their own clinical practice.

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References

1. HORROW JC, BARTKOWSKI RR. Pancuronium, unlike other nondepolarizing relaxants, retains potency at hypothermia. *Anesthesiology* 1983; **58**: 357-61.
2. D'HOLLANDER AA, DUVALDESTIN P, HENZEL D, NEVELSTEEN M, BOMBLET JP. Variations in pancuronium requirement, plasma concentration and urinary excretion induced by cardiopulmonary bypass with hypothermia. *Anesthesiology* 1983; **58**: 505-9.
3. SHANKS CA, RAMZAN IM, WALKER JS, BROWN KF. Gallamine disposition in open-heart surgery involving cardiopulmonary bypass. *Clinical Pharmacology and Therapeutics* 1983; **33**: 792-9.

Do obstetric epidurals cause continuing morbidity?

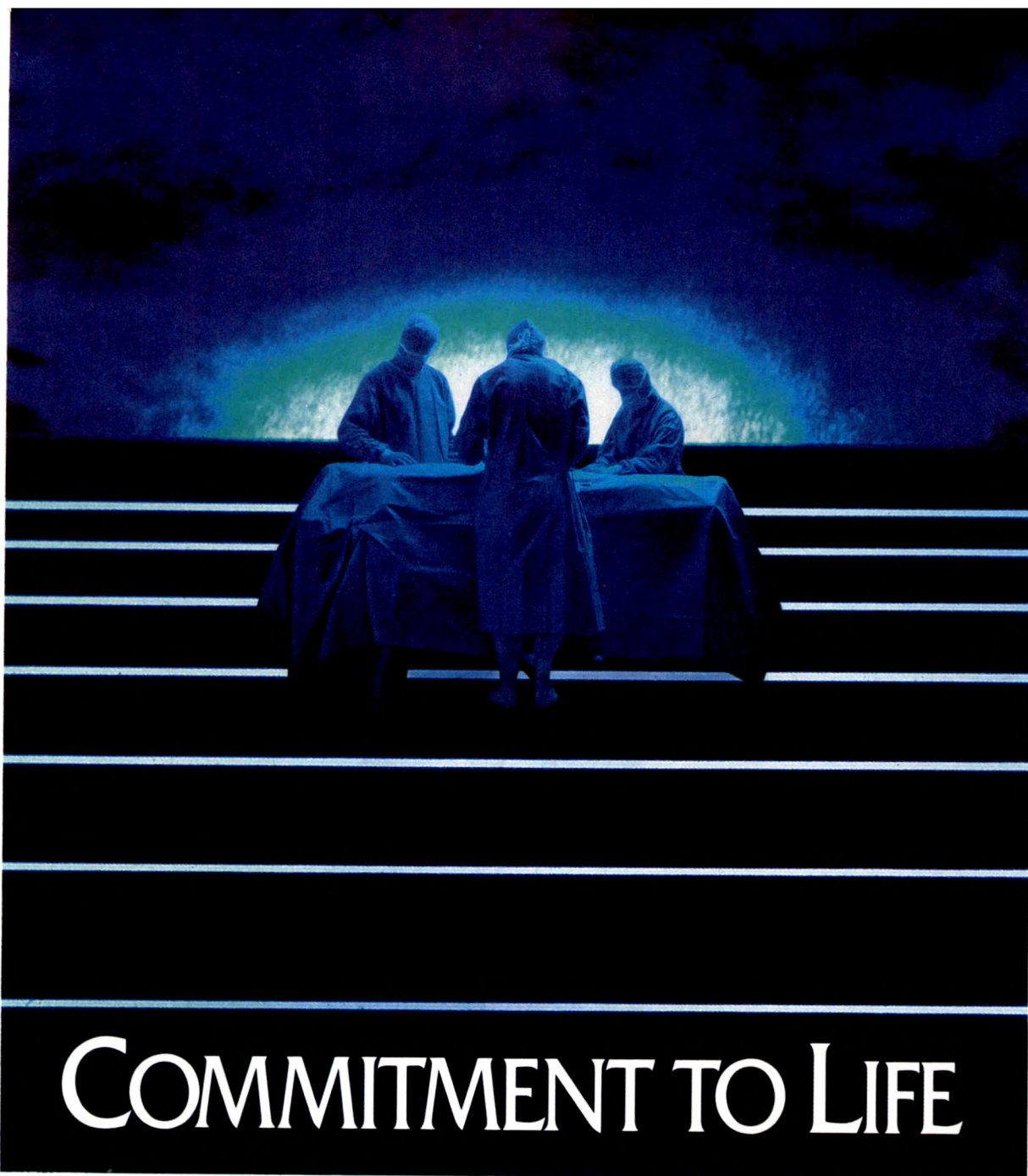
We undertook a pilot study to determine maternal morbidity after routine obstetric epidural analgesia in primiparous patients who achieved spontaneous vaginal deliveries. We surveyed 50 such patients and 50 control patients who received the usual obstetric analgesia of pethidine and promazine with Entonox for the second stage if required. Very few investigators¹⁻⁶ have considered this

subject and those who have, interviewed their patients within 6 days of delivery. These are what Crawford⁷ described as pseudocomplications. It was a prospective study.

Patients with a history of backache, headache, urinary problems, numbness and weakness in the legs before the pregnancy were excluded. The patients were given a

Table 1. Morbidity after epidural analgesia.

	2-5 days		6-8 weeks	
	Epidurals	Controls	Epidurals	Controls
Backache	12	13	15	14
Headache	2	4	11	16
Numbness in the legs	1	2	2	4
Weakness in the legs	1	1	6	4
Difficulty in walking	8	12	2	2
Urinary problems	7	7	3	5



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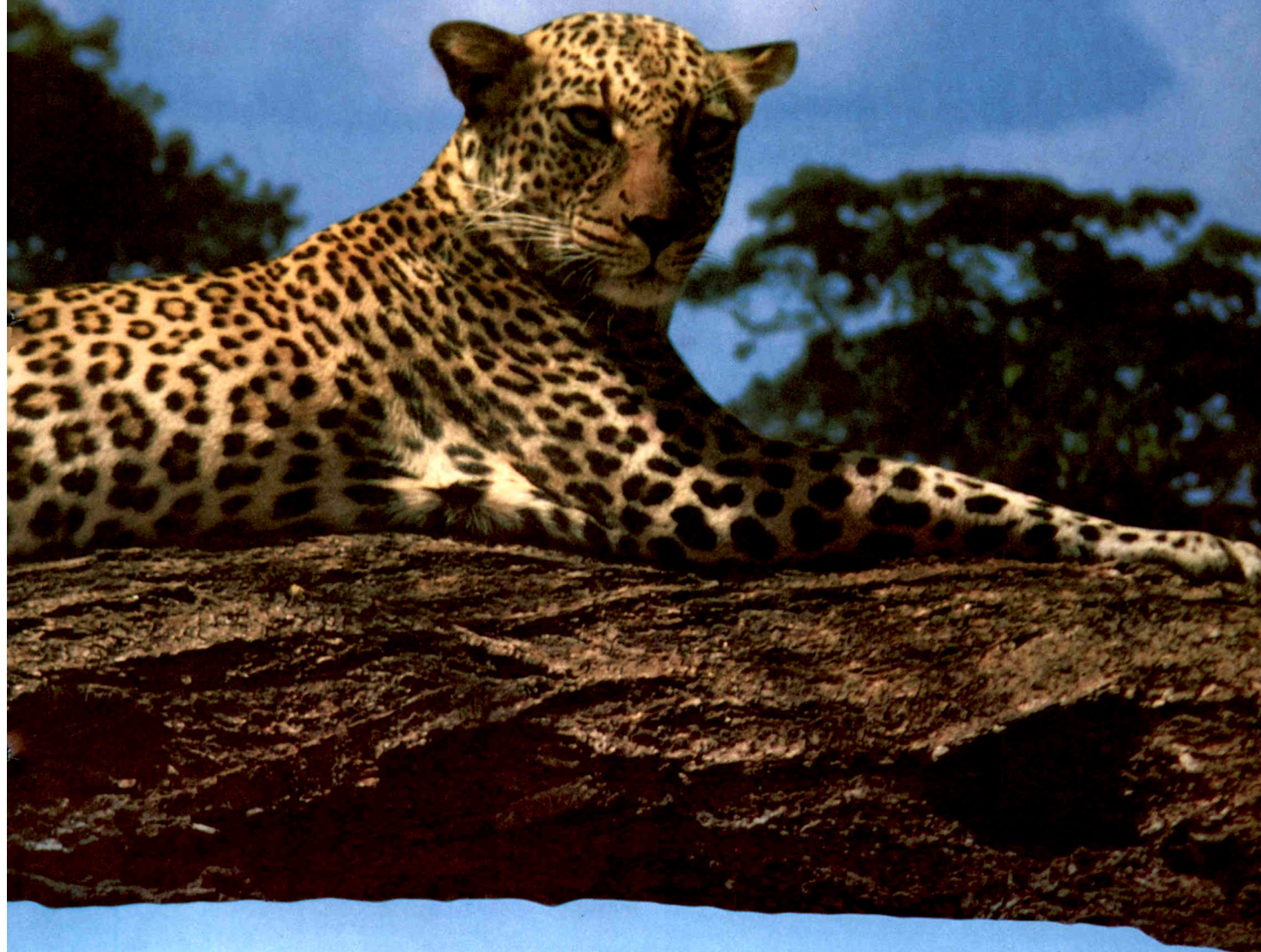
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questionnaire in the postnatal ward 2–5 days postpartum and were asked to complete the same questionnaire at home 6–8 weeks after delivery. Forty-eight of the 50 epidural patients returned the post questionnaire, so did 47 of the controls. The results are given in Table 1.

These results seem to support the view that epidural patients fare no worse than controls, and may assist anaesthetists to allay the fears of apprehensive patients. Incidentally, it was noted that of the seven patients who had an epidural vein cannulation during the course of the insertion, five complained of subsequent backache and four of them still had it at the 6–8 week period.

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Intercostal catheterisation: an alternative approach to the paravertebral space?

The paper by Mowbray, Wong and Murray (*Anaesthesia* 1987; **42**: 958–61) provides further confirmation of the utility of intercostal catheterisation for continuous analgesia of the chest wall but deserves further comment.

The authors cite our communication¹ in support of their argument and imply that intercostal catheterisation in our study resulted in extensive paravertebral spread. In fact, of nine successful blocks performed in our small series,^{1,2} only two showed evidence of spread within the paravertebral gutter although five others showed spread through an extrapleural route in combination with spread towards the paravertebral space within the intercostal space catheterised. The dye only reached the paravertebral space in two of these five subjects, and spread within the paravertebral gutter was not seen. Our study cannot therefore be used to support the contention that this is a reliable approach to the paravertebral space, and paravertebral spread is not, in my opinion, the mechanism whereby we consistently achieved analgesia over four dermatomes. It is interesting that the authors noted that catheters with a single end-hole promote medial spread. Our study was performed with such catheters, with the results outlined above, although this is a practice now abandoned in favour of a Portex Minipack, without apparent effect on the results. The stiffness of this catheter greatly facilitates its insertion but I agree that easy catheter insertion may imply misplacement.

The approach chosen, an angled medial approach from the posterior angle of the rib, is in contrast to that of many previous authors who used a classical perpendicular approach to the space and then directed the bevel of the needle laterally. This approach directs the catheter towards the paravertebral space, an effect accentuated by directing the bevel of the Tuohy needle medially, and results in extensive spread of local anaesthetic in the paravertebral space. An angled approach to the intercostal space may facilitate insertion of the catheter but, in our experience, the angle of approach makes estimation of the depth of the needle tip considerably more difficult. This may be a contributory factor to the high incidence of catheter misplacement noted by the authors.

It is a pity that all the catheters were removed immediately after surgery since this technique, whatever the route of spread, provides extensive analgesia of the chest and abdominal wall for long periods. It would seem prudent whilst experimenting with the technique to provide the patient with such benefit as may accrue.

The study from Mowbray and colleagues is a valuable

References

1. CRAWFORD JS. Lumbar epidural block in labour: a clinical analysis. *British Journal of Anaesthesia* 1972; **44**: 66–74.
2. MOIR D. *Obstetric anaesthesia and analgesia*, 2nd edn. London: Baillière Tindall, 1980.
3. MOIR DD, DAVIDSON S. Postpartum complications of forceps delivery performed under epidural and pudendal nerve block. *British Journal of Anaesthesia*, 1972; **44**: 1197–8.
4. GROVE LH. Backache, headache and bladder dysfunction after delivery. *British Journal of Anaesthesia*, 1973; **45**: 1147–9.
5. JOUPPILA R, PIHLAJANIEMI R, HOLLMEN A, JOUPPILA P. Segmental epidural analgesia and postpartum sequelae. *Annales Chirurgiae et Gynaecologiae* 1978; **67**: 85–8.
6. WEIL A, REYES H, ROTTENBERG R, BEGUIN F, HERRMANN W. Effect of lumbar epidural analgesia on lower urinary tract function in the immediate postpartum period. *British Journal of Obstetrics and Gynaecology* 1983; **90**: 428–32.
7. CRAWFORD JS. Some maternal complications of epidural analgesia for labour. *Anaesthesia* 1985; **40**: 1219–25.

addition to this literature and I agree with them that this technique deserves further investigation in a clinical setting.

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References

1. HOSIE HE, CROSSLEY AWA. A radiographic study of intercostal nerve blockade in healthy volunteers. *British Journal of Anaesthesia* 1986; **58**: 129p–30p.
2. CROSSLEY AWA, HOSIE HE. Radiographic study of intercostal nerve blockade in healthy volunteers. *British Journal of Anaesthesia* 1987; **59**: 149–54.

A reply

Thank you for the opportunity to reply to Dr Crossley and to make the following points.

Firstly, when we cited his paper¹ among others our intention was merely to demonstrate that many different opinions exist about the mode of spread.

Secondly, about the method of insertion; we disagree with Dr Crossley's description of the classical technique since both perpendicular and oblique approaches are used^{2,3} and most authors use a medially directed catheter.^{2–7} Indeed, only two papers (reporting the same study) employed a laterally directed catheter.^{1,8}

Thirdly, catheters were removed at the end of surgery since it became obvious that two catheters would be required to ensure analgesia, the second inserted ipsilaterally, superior to the wound. However, a more important reason was that our surgical wards were extremely busy and we did not consider that our patients could be appropriately monitored.

Finally, since Dr Crossley has alluded to his own papers^{1,8} we question the conclusions that he draws from them. Intercostal catheterisation is a difficult technique with no definite endpoint and our feeling is that many of the papers published have actually described intrapleural catheterisation. In Dr Crossley's papers, contrast was seen to spread from the seventh interspace to the costophrenic angle in five out of 10 volunteers. When a lateral decubitus radiograph was taken and the position of the contrast was unchanged this was taken as evidence that the contrast was deposited in an extrapleural plane. However, it has been demonstrated⁹ that when material is administered intrapleurally it is drawn to the apex, mediastinum and costo-

phrenic angle and, due to high flow resistance, is unaffected by gravity.

The position of the catheter in the intercostal space of patients in our study was ascertained without doubt—can other investigators of this technique claim likewise?

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References

1. HOSIE HE, CROSSLEY AWA. A radiographic study of intercostal nerve blockade in healthy volunteers. *British Journal of Anaesthesia* 1986; **58**: 129p–30p.
2. MURPHY DF. Intercostal nerve blockade for fractured ribs and post-operative analgesia: description of a new technique. *Regional Anesthesia* 1983; **8**: 151–3.
3. MURPHY DF. Continuous Intercostal nerve blockade for pain relief following cholecystectomy. *British Journal of Anaesthesia* 1983; **55**: 521–4.
4. O'KELLY E, GARRY B. Continuous pain relief for multiple fractured ribs. *British Journal of Anaesthesia* 1981; **53**: 989–91.
5. MIDDAGH RE, MENK EJ, REYNOLDS WJ, BAUMAN JM, CAWTHON MA, HARTSHORNE MF. Epidural block using large volumes of local anesthetic solution for intercostal nerve block. *Anesthesiology* 1985; **63**: 214–6.
6. MURPHY DF. Continuous intercostal nerve blockade. An anatomical study to elucidate its mode of action. *British Journal of Anaesthesia* 1984; **56**: 627–9.
7. JOHANSSON A, RENCK H, ASPELIN P, JACOBSEN H. Multiple intercostal blocks by a single injection? A clinical and radiological investigation. *Acta anaesthesiologica Scandinavica* 1985; **29**: 524–8.
8. CROSSLEY AWA, HOSIE HE. Radiographic study of intercostal nerve blockade in healthy volunteers. *British Journal of Anaesthesia* 1987; **59**: 149–54.

Malfunction in a needle valve

We wish to report a serious malfunction which happened in the oxygen flowmeter of an anaesthetic machine.

A Penlon IM 500 was subjected to a pre-anaesthetic check before use for a routine surgical list. When the oxygen flow control was opened the Rotameter bobbin rose to indicate a flow of 2.5 litres/minute. Further opening failed to produce an increase in flow above this level. On examination the bobbin appeared to be revolving normally in the Rotameter tube. Change of the oxygen supply from the pipeline to the reserve oxygen cylinder did not lead to an increase in flow rate. The machine was checked by the suppliers and reported to be functioning normally. However, the malfunction recurred two weeks later during a pre-anaesthetic check. The flowmeter and needle valve was dismantled on this occasion by the service engineer, and a fault discovered in the needle valve mechanism.

Normally as the oxygen flow control is opened (Fig. 1) the tapered needle (A) is withdrawn from the soft metal seating (B) and allows a variable amount of oxygen to

flow through to the Rotameter tube (D). However, in this machine when the valve was opened the soft metal seating became detached from the valve block and adhered to the needle and allowed only a limited flow of oxygen. The needle can be seen in Fig. 2 with the soft metal seating still attached (A). A normal needle is included for comparison (B).

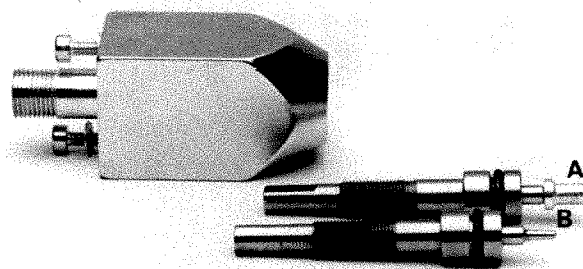


Fig. 2. Photograph of valve needle removed from block with valve seating stuck onto needle (A). A normal valve needle is also shown for comparison (B).

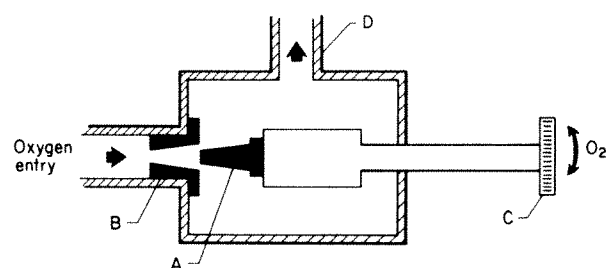


Fig. 1. Line drawing of needle valve mechanism which shows valve in open position. A, Needle; B, soft metal seating; C, oxygen flow control; D, Rotameter tube.

Fortunately this malfunction did not occur during anaesthesia and the complete needle valve mechanism was quickly replaced by the manufacturers. This incident, however, brings to light yet another cause of equipment malfunction and once again emphasises the need to check all equipment thoroughly before use.

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Total spinal anaesthesia for a Jehovah's Witness with primary aldosteronism

A 33-year-old female Jehovah's Witness who weighed 45 kg complained of intermittent hypertension (systolic over 160 mmHg) with moderate headache since 1982. She complained again of hypertension (systolic over 210 mmHg) in 1985 and was treated with antihypertensive drugs and referred to our University clinic. A diagnosis of primary aldosteronism was made after detailed examination.

An aldosterone-producing tumour of the left adrenal gland was removed under total spinal anaesthesia in January

1986. An epidural catheter was inserted at L₃–L₄ into the subarachnoid space and the tip of the catheter located at the L₁–L₂ level. The trachea was intubated after intravenous injection of thiopentone 250 mg and suxamethonium 40 mg, and oxygen 3 litres/minute and nitrous oxide 2 litres/minute inhaled. Twenty millilitres 2% carbocaine was injected through the catheter at a rate of 0.1 ml/second in divided doses.

A Swan-Ganz catheter was inserted for cardiovascular

monitoring. The arterial blood pressure decreased to 80/50 mmHg minutes after injection of carbocaine. SVO_2 of the mixed venous blood was about 75% throughout the procedure.

The intra-operative course was smooth and intra-operative muscle relaxation excellent. She recovered consciousness 3 minutes after withdrawal of nitrous oxide. Her postoperative course was also uneventful.

Plasma aldosterone levels increased markedly during manipulation of the tumour and then decreased gradually to the normal level after its removal. Plasma ACTH and cortisol concentrations were elevated significantly by surgical intervention while adrenaline, noradrenaline and dopamine in the plasma remained within normal ranges.

This method has been used widely since 1969 in many pain clinics in Japan to treat various pain syndromes. Total spinal anaesthesia is often considered to be the most dangerous complication following spinal anaesthesia and epidural anaesthesia but the method can be applied safely in clinical practice, provided that adequate care is taken of the cardiorespiratory systems.

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Recurarisation after vecuronium?

The case report by Cody and Dormon (*Anaesthesia* 1987; 42: 993-5) which described recurarisation after vecuronium in a patient with renal failure, deserves further comment. Several points remain unanswered.

They report that the patient's drug therapy included nifedipine, ranitidine and insulin but they omit to mention whether she was on any antibiotic therapy for her infected ulcer and osteomyelitis of her left leg. It is well recognised that many antibiotics (not only the aminoglycosides) may augment neuromuscular block¹ and at the same time change the characteristics of the block in such a way that neostigmine is inadequate as a reversal agent. Intravenous calcium would perhaps have been a more appropriate therapeutic manoeuvre if this was the case.

She was also noted to have a pre-operative metabolic acidosis (bicarbonate 7 mmol/litre) compatible with her chronic renal failure. This was presumably associated with respiratory compensation and yet her lungs were ventilated to normocapnia during her anaesthetic. A diagnosis of recurarisation by vecuronium due to severe acidosis was made but it is obvious from her postoperative arterial blood gas analysis that this was a mixed acidosis with Paco_2 6.8 kPa. However, her lungs were still ventilated inadequately (Paco_2 6.0 kPa) several minutes later after tracheal intubation (presumably without a relaxant), assisted ventilation and an attempt to correct her metabolic acidosis.

The suggestion that metabolic acidosis interferes with neostigmine antagonism of non-depolarising muscle relaxants has not been substantiated. Miller *et al.*² found that metabolic alkalosis but not metabolic acidosis limited neostigmine antagonism of a tubocurarine neuromuscular blockade. Respiratory acidosis did, however, limit antagonism.

Renal excretion accounts for approximately 50% of the clearance of neostigmine³ in anaesthetised patients. The excretion of the older, long-acting non-depolarising muscle relaxants is decreased in renal failure. However, the magnitude of the decrease in anticholinesterase clearance exceeds even that reported for these longer-acting muscle relaxants. Therefore, the muscle relaxant will probably not outlast the antagonist drug in a patient with renal failure. Reports of recurarisation in anephric patients are more likely to be due to interaction between drugs such as antibiotics and diuretics with residual muscle relaxant activity. Such interactions are not well antagonised by the anticholinesterase drugs and can produce weakness and respiratory insufficiency despite adequate concentrations of the antagonist drugs.⁴

Theoretically, it seems highly unlikely that vecuronium, a drug which depends predominantly on the biliary system for its elimination, was a cause of recurarisation in this case report, particularly in view of its intermediate duration

of action and pharmacokinetics and pharmacodynamics that differ little between normal patients and those in renal failure.⁵

Further questions remain. Neuromuscular blockade was assessed by response to a supramaximal train-of-four stimulation to the ulnar nerve. What type of monitor was used, how was supramaximality obtained and is it possible that direct muscle stimulation was observed? Finally, why did it take over 20 minutes after a diagnosis of depressed neuromuscular function, to give a second dose (2.5 mg) of neostigmine?

This is an interesting case report but there are too many unknown factors to attribute this patient's respiratory depression conclusively to vecuronium recurarisation. A more controlled study is required.

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References

1. PITTINGER C, ADAMSON R. Antibiotic blockade of a neuromuscular function. *Annual Review of Pharmacology* 1972; 12: 169-84.
2. MILLER RD, VAN NYHUIS LS, EGER II EI, WAY WL. The effect of acid-base balance on neostigmine antagonism of d-Tubocurarine-induced neuromuscular blockade. *Anesthesiology* 1975; 42: 377-83.
3. CRONNELLY A, STANSKI DR, MILLER RD, SHEINER LB, SOHN YJ. Renal function and pharmacokinetics of neostigmine in anaesthetised man. *Anesthesiology* 1979; 51: 222-6.
4. CRONNELLY R. Kinetics of anti-cholinesterases. In: NORMAN J, ed. *Clinics in anaesthesiology. Neuromuscular blockade*. London: W.B. Saunders, 1985: 315-28.
5. FAHEY MR, MORRIS RB, MILLER RD, NAUYEN TL, UPTON RA. Pharmacokinetics of Org NC45 (Norcuren) in patients with and without renal failure. *British Journal of Anaesthesia* 1981; 53: 1049-52.

This is a comment about the case report by Cody and Dormon (*Anaesthesia* 1987; 42: 993-5) of recurarisation after vecuronium in a patient with renal failure. It is certainly true that acidosis interferes with the reversal of a non-depolarising neuromuscular blockade but this is not, in my opinion, the sole explanation. We have shown in our laboratory, using an isolated rat phrenic nerve diaphragm preparation, that doxapram has a biphasic action at the neuromuscular junction. Neuromuscular transmission is enhanced by doxapram but doxapram itself produces neuromuscular blockade in the presence of a subparalytic dose of a non-depolarising muscle relaxant (data presented to the European Academy of Anaesthesiology, September

1987). A bolus dose of doxapram 1 mg/kg distributed throughout the plasma should result in an initial concentration of approximately 20 µg/ml and a concentration of approximately 5 µg/ml could result if this were finally fully distributed throughout the extracellular fluid. The threshold concentration required to produce neuromuscular blockade in the presence of a subparalytic dose of relaxant *in vitro* is about 20–40 µg/ml. It could therefore be that the bolus dose of doxapram which the patient received was responsible and precipitated the episode of recurarisation. The relationship between time and event as described is compatible with this possibility.

Nerve stimulators are nowadays relatively cheap and easy to use. They should therefore be an integral part of every anaesthetic which includes the use of a muscle relaxant, especially if one of the newer, shorter-acting agents is in use.

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A reply

Thank you for the opportunity to reply to the comments of Drs Scott and Pollard. Dr Pollard's comments are interesting but they have not been substantiated in a clinical situation and we consider that there is little relevance of the rat diaphragm preparation to the case we report.

Recurarisation after vecuronium in a patient with renal failure

The recent article by Cody and Dormon (*Anaesthesia* 1987; 42: 993–5) suggested that vecuronium produced recurarisation in a renal failure patient. The authors claimed that the clinical picture they observed was due to delayed excretion of vecuronium which was further complicated by respiratory and metabolic acidosis. They concluded that 'doubts may be raised about the suitability of vecuronium in renal failure'. I have personally administered vecuronium to hundreds of patients with renal failure and I cannot support the authors' concerns about vecuronium in these patients. The doses of vecuronium used in this patient appear to be excessive. The initial intubation dose was greater than 0.1 mg/kg and recovery from this dose occurred with impressive speed. These facts suggest that neuromuscular monitoring may have been inaccurate (i.e. monitoring of movement of fingers other than the thumb) and thus allowed a significant overdose of vecuronium in a sick patient. If monitoring were accurate (i.e. only thumb twitch used), then the impressive recovery from the large intubation dose suggests that the additional dose would be

In reply to Dr Scott's comments, the antibiotic used was of the penicillin group and to our knowledge this group does not produce any effect on neuromuscular blockade. However, if the prolonged blockade was contributed to by the antibiotic it is the second case to do so.¹

As Dr Scott points out, neostigmine may not be the agent of choice to reverse a block potentiated by antibiotics and acidosis. Neostigmine initially produced adequate reversal and return of the train-of-four response in this patient. The problem was of recurarisation. Neostigmine proved to be the agent of choice to effect a reversal when the acidosis was corrected, which strongly suggests recurarisation due to acidosis.

Lastly, the reason a second dose of neostigmine was given after 20 minutes was that a diagnosis of cause (acidosis) was first established and then appropriate treatment (with bicarbonate) instituted before the dose of neostigmine was repeated.

Hammersmith Hospital,
London W12 0HS

M. CODY
F.M. DORMON

Reference

1. KRONENFELD MA, THOMAS SJ, TURNDORF H. Recurrence of neuromuscular blockade after reversal of vecuronium in a patient receiving polymyxin/amikacin sternal irrigation. *Anesthesiology* 1986; 65: 93–4.

handled in similar fashion such that recurarisation post-operatively from vecuronium would be highly unlikely.

The introduction of vecuronium and atracurium has revolutionised the anaesthetic management of renal failure patients at our institution where over 300 kidney transplants/year are performed. Recurarisation was common with the use of pancuronium and tubocurarine but it is now uncommon at our institution; when it has occurred with these two relaxants, an overdose has invariably been administered, usually because of inaccurate neuromuscular monitoring.

In summary, I suggest that vecuronium be viewed as a muscle relaxant of choice in patients with renal failure with the understanding that muscle relaxants in any patient must be used intelligently, particularly in patients with metabolic organ disease.

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USA

M.R. FAHEY

Spurious plasma electrolyte results

It is well known that spurious serum electrolyte results are obtained when blood is taken from an arm which has intravenous fluid flowing into it. This report describes a similar source of error when blood aspirated from an external jugular vein produced very abnormal results.

A 72-year-old man with a 3-day history of large bowel obstruction, underwent laparotomy 12 hours after admission. Pseudo-obstruction was diagnosed intra-operatively and 2.5 litres of fluid were removed from the gastrointestinal tract by Savage decompression and nasogastric aspiration. Hypokalaemia was suspected when U-waves appeared on the ECG.

An infusion of 0.9% saline with 20 mmol/litre potassium

chloride was commenced via a 16-SWG cannula in the left forearm, and 5 ml blood aspirated for the purpose of urea and electrolyte estimation, from the prominent left external jugular vein using a 21-SWG needle (the patient was lying flat and supine).

The electrolyte results showed a plasma potassium of 9 mmol/litre (Table 1); two separate estimations were performed on the same unhaemolysed sample and gave similar results. Thus hyperkalaemia was unexpected so a further blood sample was taken from the right arm and this indicated a plasma potassium of 5.1 mmol/litre which was considered to be consistent with the clinical situation.



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Table 1. Plasma electrolytes (mmol/litre).

Time	Site	Urea	Potassium	Sodium	Chloride
2 hours pre-operatively	Right arm	14.7	4.2	140	110
Intra-operatively	Left external jugular vein	10.7	9.0	142	130
1 hour later	Right arm	14.2	5.1	143	110

It is concluded that if intravenous fluids are given rapidly into the left arm then blood aspirated from the left external jugular vein may be contaminated with intravenous fluids and may lead to clinically important errors. It is advisable therefore that rapidly running infusions are stopped tem-

porarily when blood is sampled from ipsilateral neck veins or centrally placed venous catheters.

Waveney Hospital,
Ballymena,
Northern Ireland

D.A. ORR

False positive test dose and epidural fentanyl

Lignocaine 2% 2 ml is recommended as an epidural test dose in obstetrics for the detection of subarachnoid catheter placement.¹ This is a report of an intensive care case in which this test dose was used but signs of local anaesthetic block suggestive of subarachnoid catheter placement, developed only after the opioid was injected. Fortunately, the patient did not develop respiratory depression and the duration of analgesia was short.

A low thoracic epidural was performed on a 56-year-old woman with multiple rib fractures. The dura was accidentally punctured. The needle was withdrawn until the flow of cerebrospinal fluid (CSF) stopped, and a catheter introduced. There was no flow of CSF down the catheter. Lignocaine 2% 2 ml was used as a test dose and there were no signs of subarachnoid block at 10 minutes.

Fentanyl 50 µg in 5 ml saline was injected through the catheter. The patient complained of leg weakness after 20 minutes. Examination revealed loss of sensation below T₈, with weakness in the hip flexors. Detailed testing of sensation was not attempted but both legs were noted to be warm and movement of the feet was unaffected. These signs were transient and no hypotension, loss of consciousness or respiratory depression occurred. A similar dose of fentanyl was given when pain returned 2 hours later; the sensory and motor changes did not recur.

An epidural infusion of fentanyl 7.5 µg/ml at 4 ml/hour was used for 48 hours. The patient stayed in the intensive care unit. The respiratory rate remained above 16 breaths/minute, she remained conscious and analgesia was satisfactory.

The test dose gave a false positive indication that the catheter was misplaced. This impression was confirmed by chest X ray after contrast medium had been injected through the catheter. Contrast medium appeared in the epidural space but there was no subdural or subarachnoid

spread. The late onset of false positive signs after a test dose is explained thus. The test dose consisted of lignocaine 2 ml. A further 1 ml primed the Portex epidural filter² and was subsequently flushed into the epidural space. The total dose of lignocaine was 60 mg and the volume and concentration was 7 ml of 0.86%, possibly enough to give an epidural block. The volume may have been altered further by CSF which leaked through the dural puncture.

Bromage³ showed that epidural lignocaine 60 mg via the lumbar route blocked only three or four segments and that the extent of block was independent of volume of solution, but these alternative explanations (subarachnoid or subdural block) are not supported by the X ray finding or the latency of onset. Extensive epidural spread in the case described here could be attributed to thoracic administration. Assuming that the sensory and motor block was due to the dilution of the epidural test dose I suggest that the patient must be warned of weakness and that the filter should be cleared of local anaesthetic. The volume of solution which contains opioid may determine the extent of dilution and segmental spread of the test dose. If a dural puncture is possible, the consequences of dilution of the test dose by CSF should be appreciated.

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A.M. SEVERN

References

1. PRINCE G, MCGREGOR D. Obstetric epidural test doses. A reappraisal. *Anaesthesia* 1986; **41**: 1240-50.
2. OYSTON J. Priming volume of epidural equipment. *Anaesthesia* 1986; **41**: 554.
3. BROMAGE PR. *Epidural analgesia*. London: W.B. Saunders, 1978: 142-7.

Palsy after femoral nerve block

Much has been written about nerve injury to the brachial plexus after brachial plexus block but very little about femoral nerve injury after femoral nerve block. This is a report of two cases of femoral nerve palsy.

Femoral nerve blocks were performed after the induction of general anaesthesia in a series of 27 consecutive arthroscopies. The femoral nerve was located with the nerve stimulator described by Smith¹ and 10 ml 0.5% bupivacaine injected through a 21-gauge Gillette hypodermic needle.

Postoperative analgesia was satisfactory in all 27 patients but two patients developed a prolonged complete femoral nerve palsy with quadriceps paralysis and anaesthesia over the anterior aspect of the thigh. Neither patient was

investigated with nerve conduction studies; both were given physiotherapy and both showed spontaneous full recovery within 10 days. The most likely cause of such a prolonged block was intraneural injection of the local anaesthetic, or possibly direct damage to the nerve with the needle.²

A nerve stimulator allows very accurate localisation of the femoral nerve and it may be considered wise to reposition the needle once quadriceps contraction is elicited. The use of a short, bevelled (blunt) needle might also help one to detect inadvertent neural puncture since tissue planes are then easily identified. Were the block to be performed in an awake patient, intraneural injection might be expected to be painful.

It would be interesting to know if this is a more commonly encountered problem than the lack of published literature implies.

Northampton General Hospital,
Northampton, NN1 5BD

C.M. FRERK

References

1. SMITH BE. Distribution of evoked paraesthesiae and effectiveness of brachial plexus block. *Anaesthesia* 1986; **41**: 1112-5.
2. SELANDER D, EDSHAGE S, WOLFFE T. Paresthesiae or no paresthesiae? Nerve lesions after axillary blocks. *Acta Anaesthesiologica Scandinavica* 1979; **23**: 27-33.

Towards safer intravenous regional anaesthesia

The popularity of intravenous regional anaesthesia (IVRA) as a technique has waxed and waned since its conception by August Bier in 1908.¹ There is general agreement among anaesthetists and casualty surgeons on the local anaesthetic to be used and the training of proponents of IVRA both in the technique and in resuscitation of the patient in event of complications. The tourniquet systems used at various hospitals to achieve IVRA seem to be the remaining weak link in the chain towards safer IVRA, and this is supported by the five serious incidents that involved automatic tourniquets which prompted the DHSS to issue Hazard Notice HN (82)7.

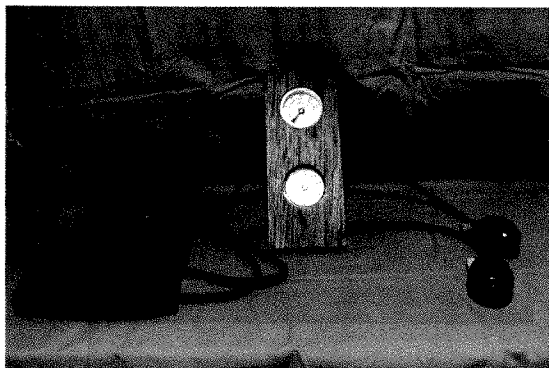


Fig. 1. The tourniquet system.

We wish to report a tourniquet system designed and constructed by one of us (M.H.) with safety in mind, which has been used in more than 200 cases over 4 years by anaesthetists of all grades with no complications due to the tourniquet.

The system consists of two OEC gauges, two hand inflation bulbs and valves, a Thackray double cuff and a wooden gague mounting block with metal angled backplate and stand (Fig. 1). The gauges register cuff pressure at all times and tube joints are sealed with rubber compound and cable ties for security. A double cuff technique (Hoyle²) can be used with this system without two-way taps or compressed gases, while the pressure in both cuffs is monitored continuously.

The cost of the system is currently £130 for parts and we believe the system to be both simple and safe.

Princess Alexandra Hospital,
RAF Wroughton,
Wiltshire

M. HICKS
S.J. HUNTER

References

1. BIER A. Ueber einen neuen Weg Localanästhesie an den Gliedmaassen zu erzeugen. *Archiv für Klinische Chirurgie* 1908; **86**: 1007-16.
2. HOYLE JR. Tourniquet for intravenous regional analgesia. *Anaesthesia* 1964; **19**: 294-6.

Arterial cannulation

The Seldinger technique is popular for arterial cannulation but often spreads blood about. If the tip of the needle is only just within the artery then it may be displaced while one finds the wire and inserts it. A modified technique avoids both problems.

The arterial puncture is made with the wire partly inserted into the needle—the tip about half way down the shaft—and retained by the ring or little finger against the palm. This adds no significant difficulty to handling the

needle. The flashback is easily seen but a jet of blood is avoided.

Those anaesthetists who use a syringe barrel as a handle could pre-insert the wire and thus avoid movement of the needle.

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A.K. MIDGLEY

Passage of nasogastric tubes

The standard method to pass a nasogastric tube in the anaesthetised patient is to insert a nasotracheal tube through the nose into the oesophagus and then to thread the nasogastric tube through this. Unfortunately, many nasogastric tubes are fitted with connectors at the proximal end which are larger in diameter than the internal diameter of the tracheal tube. Thus, the tracheal tube can be removed only if a longitudinal slit is made through the wall.

A simple technique which obviates the need for a nasal tube is to pass the well-lubricated 16-FG nasogastric tube

through the nostril whilst the neck is held in maximum flexion. I have had no failures with this technique on the last 36 consecutive occasions although on two occasions I had to deflate the tracheal tube cuff to permit passage down the oesophagus. It is, of course, important to ensure that the tracheal tube is not kinked or displaced whilst this manoeuvre is performed.

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M.K. SYKES

Intravenous sedation for cataract surgery and ketamine

Drs Gilbert *et al.* (*Anaesthesia* 1987; 42: 1063-9) suggest a satisfactory technique for intravenous sedation for cataract surgery. They are to be congratulated. Sedation for cataract surgery is difficult and frequently unrewarding. Patients who are too lightly sedated may find their degree of awareness unacceptable; patients who are too deeply sedated may lose control of their airways and patients in between are frequently restless and confused, which makes the surgery difficult.

My arrangement with the eye surgeons with whom I work is that patients receive either a general anaesthetic or a local without any sedation. This avoids the above problems. However, there are patients who are reluctant to accept a local analgesic technique without sedation and who are unfit for general anaesthesia. Over the last 18 months I have been involved with four such patients of ASA grade 4 with exercise tolerance that ranged from 5-50 paces on the level. These patients were chronic bronchitics who were able to tolerate a supine, or nearly supine position for 30 minutes.

Local analgesia was supplemented with midazolam and ketamine sedation. The patients were brought to theatre

after oral premedication with diazepam 10 mg and metoclopramide 10 mg. Oxygen 2-3 litres/minute was administered through a nasal cannula. Midazolam 2 mg and ketamine 50 mg were then given intravenously. The surgeon administered a retrobulbar and facial nerve blocks and surgery commenced. Sedation was supplemented by ketamine 25 mg every 5 minutes until surgery was finished.

This technique produced good operating conditions for the surgeon and complete amnesia for the patient. There were no airway problems and all patients were able to respond verbally within 6 minutes of the end of surgery.

Strictly this is an anaesthetic technique rather than a sedative technique since the patients are unresponsive throughout the procedure but it is probably quite inadequate for cataract surgery. Incidentally, the retrobulbar block produces a soft eyeball and the notion that ketamine should not be used for cataract surgery because it might raise the intra-ocular pressure, is groundless.

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W. KONARZEWSKI

Modification of Macintosh laryngoscope for difficult intubation

Drs Callander and Thomas (*Anaesthesia* 1987; 42: 671) are correct in their claim that difficulty at tracheal intubation in patients with limited mouth opening can frequently be overcome by use of a modified Macintosh laryngoscope. The blade curved more shallowly at its proximal part, made smaller in the horizontal plane and bent slightly at the tip,¹ has been used effectively in selected patients in our department since 1982.

Holbaek Centralsygehus,
4300 Holbaek,
Denmark

M. IBLER

Reference

1. IBLER M. Modification of Macintosh laryngoscope blade. *Anesthesiology* 1983; 58: 200.

Inspired monitoring

Monitoring of the inspired oxygen concentration is now well established and regarded as both reasonable¹ and essential,² especially when a circle system is in use. Safety is enhanced since the low alarm warns of upstream disconnections and of failure or contamination of the inspired oxygen source.

The oxygen analysers currently available have both low and high alarms. Perhaps because of the irritation caused by inappropriate auditory alarms, the anaesthetist rarely makes use of the high alarm but, if the high alarm is carefully adjusted to sound fractionally above the chosen oxygen percentage, it will alert the anaesthetist to any event which increases the apparent oxygen concentration. Thus the alarm will sound if there is a reduction in supply of nitrous oxide, or a disconnection or fault in the vaporizer. Accidental addition of extra oxygen by, for instance, mistaken use of the oxygen flush system will be detected

immediately. The high alarm also detects the reduction of vapour concentration which results from unobserved emptying of the vaporizer. This is of great importance if the fashion is followed to abstain from use of nitrous oxide and to rely solely on high concentrations of a volatile anaesthetic agent to ensure unconsciousness.

We urge anaesthetists to make use of the full facilities of these commonly available devices to enhance patient care.

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Oxford OX2 6HE

I. SIVAKOLUNTHO
C.E. BLOGG

References

1. MATHIAS JA, LUNN JN. Minimal monitoring and vigilance. *Anaesthesia* 1987; 42: 683-4.
2. SYKES MK. Essential monitoring. *British Journal of Anaesthesia* 1987; 59: 901-12.

Pain-free injections

The letter by Dr Porteous (*Anaesthesia* 1987; 42: 1021) advocates a somewhat complicated method to reduce the pain caused by injection of propofol or methohexitone into peripheral veins such as the dorsum of the hand.

Anaesthetists until fairly recently routinely injected at the antecubital fossa and the move to the dorsum of the hand was prompted only by the increasingly perceived need to maintain an open vein during anaesthesia with winged needles. There are now self-sealing, flexible indwelling cannulae available at a similar cost and these do not allow

extravasation when left in the antecubital fossa. In my experience, this route offers almost 100% pain-free injection of propofol and has the additional advantage that it avoids the small but unsatisfactory incidence of visible bruising and painful thrombophlebitis on the dorsum of the hand.

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D.J. LINTIN

Weals after propofol

Propofol has many advantages as an anaesthetic induction agent and one of its attractions is the low incidence of allergic reactions¹ but this is a report of a case in which signs of local histamine release occurred after injection of propofol.

A 33-year-old man presented for outpatient cystoscopy. He was fit and had no specific allergies although he suffered from mild summer hay fever.

A 20-gauge cannula (Venflon) was sited in a vein in the dorsum of his left hand and propofol 150 mg injected slowly. The patient complained of pain in his hand shortly before he lost consciousness but no abnormality was noted on examination. Anaesthesia was continued with nitrous oxide, oxygen and enflurane. No other intravenous drugs were given. A weal and flare reaction appeared on the dorsum of the hand and forearm over the next 1–2 minutes. No signs of generalised histamine release were noted and the anaesthetic continued uneventfully.

The weal and flare reaction persisted for about 30 minutes but the arm looked and felt normal when the patient was ready for discharge 2 hours after anaesthesia.

Pain on injection is common with propofol although the

incidence varies the site of injection.² There have been some reports of erythema, non-specific rashes and phlebitis^{1–3} but I am unaware of any previous reports of weals which may indicate local histamine release.

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H.A. AITKEN

References

1. DOENICKE A, LORENZ W, STANWORTH D, DUKA TH, GLEN JB. Effects of propofol ('Diprivan') on histamine release, immunoglobulin levels, and activation of complement in healthy volunteers. *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 15–20.
2. STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 152–6.
3. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA, STEPHENSON JK. Dose requirements of ICI 35,868 (Propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; 39: 1168–71.

Hallucinations after propofol

It was interesting to read Dr Lloyd's report of a patient who had hallucinations after a propofol anaesthetic (*Anaesthesia* 1987; 42: 1015–6) since I have witnessed a similar episode myself. The patient was a fit, but slightly anxious, 58-year-old man who underwent day-case anaesthesia for manipulation of lumbar spine. Premedication was not given. Induction was with propofol 175 mg and maintenance with nitrous oxide, oxygen and halothane, and a further 25 mg propofol. He rapidly regained control of his airway but became very distraught and clammy on return to the recovery area. He sat rigidly upright, stared ahead unseeing, crossed himself and shouted 'rank and number'. He appeared to be terrified and was oblivious to attempts to soothe him. He relaxed and became communicative after about 10 minutes. He denied any memory of unpleasant dreams. This episode was in marked contrast to the usual pattern of emergence from propofol anaesthetics, from which patients awake in a mildly euphoric state of mind. Fortunately, although it was unpleasant to witness, the patient had no recollection of anything untoward.

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V.M. NELSON

It is neither their specialty nor their hospital that tickled the fancy of Drs Hunter, Thornily and Whitburn's patients. A female patient whom I recently anaesthetised with propofol for an orthopaedic procedure spent the next half hour loudly shouting for her orthopaedic surgeon in an unmistakably amorous manner.

This caused much hilarity among the theatre staff; however, perhaps there could be more serious implications. Older anaesthetists may remember an incident widely reported in the popular press several years ago, in which an unchaperoned single-handed operator-anaesthetist who used propanidid for anaesthesia for fitting an intra-uterine contraceptive device was accused by the patient of raping her under the anaesthetic.

Perhaps an extra function of our trained anaesthetic assistants should be that of chaperone.

*Cheltenham General Hospital,
Cheltenham,
Glos. GL53 7AN*

P.N. YOUNG

The staff at the Middlesex Hospital are not alone in having their attractiveness to the opposite sex enhanced by propofol (*Anaesthesia* 1987; 42: 1128–9). The majority of our patients, as in the experience of Dr Hunter and his colleagues, have been female and have undergone a short procedure, usually dilatation and curettage. Male patients are, however, not immune and our recovery room staff report that, while they are impressed with the rapid recovery from propofol, they find fending off the amorous advances irksome. We wonder whether aphrodisiac can now be added to the list of properties of the drug.

Our findings relate to short cases. We would be interested to know if staff of intensive therapy units are presented with such boisterous and attentive patients when propofol is used for sedation over long periods.

*The Princess of Wales RAF Hospital,
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Cambs. CB6 1DN*

D.G. SMYTH

P.J. COLLINS-HOWGILL

We read with interest the letter entitled 'Arousal from propofol.' We have induced anaesthesia with propofol in over 300 patients, predominantly male, with an age range of 19–90 years for routine urological surgery. All the patients were visited postoperatively on the ward and not one of them volunteered any recollection of erotic dreams or indeed made any advances of a sexual nature.

In a further series, 40 patients induced by a woman anaesthetist were specifically questioned postoperatively about

dreams. One of these patients did admit on close questioning that he had dreamt about his anaesthetist but he refused to elaborate on the nature of his experience.

We wonder whether it was the good looks of our colleagues at the Middlesex or maybe the surgical stimulation involved which promoted the reported uninhibited female behaviour and whether the incidence of this phenomenon could be reduced by an increased propofol dosage.

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K.D. THOMSON
A.B. KNIGHT

Drs Hunter, Thornily and Whitburn may rest easy: it is not only Middlesex Hospital anaesthetists who provoke unsolicited attentions after the use of propofol (*Anaesthesia* 1987; 42: 1128-9). I have had similar experiences in the course of about 200 recent propofol anaesthetics for minor gynaecological surgery. Amorous and disinhibited behaviour did not occur after laparoscopy (using a technique that involved propofol and alfentanil without tracheal intubation) but was a problem in more than 12% of the

130 propofol/alfentanil anaesthetics given for procedures such as dilatation and curettage, cystoscopy and cervical biopsy and diathermy. I also have been embraced on occasion but the commonest feature is to be mistaken for the patient's normal partner.

Colleagues have found much the same and initially the phenomenon provided a source of some amusement without seeming significant enough to warrant any attempt at formal study. However, in the light of the perennial problem of allegations of sexual impropriety which is emphasised again in the latest report of the Medical Defence Union¹ it may prove prudent to ensure that a female third party is always present during the induction of and emergence from propofol anaesthesia, particularly when this is for gynaecological or genito-urinary procedures which are not inherently painful.

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Liverpool L9 1AE

S.R.W. BRICKER

Reference

1. Anonymous. 'No chaperon'. *The Medical Defence Union Annual Report* 1987; 50.

Book reviews

- Drugs in anaesthesia: mechanisms of action** 172
 Edited by S.A. FELDMAN, C.F. SCURR AND SIR
 WILLIAM PATON
A synopsis of anaesthesia, 10th edn. 172
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Drugs in anaesthesia: mechanisms of action

Edited by S.A. FELDMAN, C.F. SCURR AND SIR WILLIAM PATON. Pp. 456. Edward Arnold, 1987. £50.00.

This unusual book deals primarily with the mechanisms of action of drugs used in anaesthesia and intensive care. It is not intended to be a comprehensive pharmacology text and its objective is rather to provide a framework of basic scientific data and principles on which detailed information about specific drugs can be built to promote their safer and more effective use. The impressive cast of authors includes clinicians and academic and industrial pharmacologists, physiologists and biochemists. Most are from the UK but the USA, Australia and The Netherlands are also represented.

The first four general chapters are devoted to receptors and their actions, pharmacokinetics, transfer of drugs across biological membranes and the effects of anaesthesia on drug disposition. The main section of 12 chapters under the heading of 'Specific mechanisms of action', covers hypnotics, general and local anaesthetics, neuromuscular blockers, autonomic drugs, analgesics, antihistamines, hypotensive agents and channel blockers. The final part consists of four oddly named 'Appendices' on toxicity, drug measurement, mechanisms of drug interaction and steady state pharmacology.

Many of the contributions are outstanding and make almost compulsive reading. The chapters on receptors, general anaesthesia, local anaesthesia and neuromuscular blockade deserve special mention in this respect. The book is attractively produced with good illustrations and an adequate index, and is generally well referenced. Inevitably, there are shortcomings. Detail is excessive at times, the chapter on non-opiate analgesics and prostaglandins seems to be curiously detached and irrelevant, and that on hypotensive agents is unbalanced. The appendices would have been better expanded to do justice to their topics. The section on toxicity is so limited as hardly to justify inclusion, and the bare technicalities of drug measurement are of little relevance either to mechanisms of action or to anaesthetic practice. There is no mention of naloxone in the appendix on interactions, nor of the potentiation of drugs such as morphine and diazepam by cimetidine. The frequent use of unfamiliar abbreviations is irritating and there is some repetition. Pharmacokinetic discipline is often lax and statements such as 'metabolism probably contributes to the plasma clearance of about 20% of an injected bolus does ...' (p. 175) should never have been allowed.

These are minor criticisms, however, and the editors are to be congratulated on the production of a book which contains a wealth of useful information and

provides a new dimension of insight into the mechanisms of action of these drugs. The most important advances in anaesthesia in recent years have come not from the introduction of new drugs but from the better use of existing agents. Such progress has been made possible only by increased awareness of their effects, the application of pharmacokinetic principles and better understanding of the mechanisms of action. The book carries the right message at the right time and will be of great value not only to practising anaesthetists but also to basic scientists and others who are interested in these drugs. This model approach could be extended to drugs used in other medical specialties with great benefit.

L.F. PRESCOTT

A synopsis of anaesthesia, 10th edn

R.S. ATKINSON, G.B. RUSHMAN AND J.A. LEE. Pp. 898 (835 + index). Wright, 1987. £25.00.

The authors have made considerable changes in the latest edition of this established text which, for me, have made the book far more readable. Gone is the white-coat pocket, soft-covered edition with irritatingly small print. The 10th edition is now hard-backed and measures 24 × 16.5 cm. The quality of both the paper and print have been improved considerably, with an increase of only 8 lines per page, which results in a much more readable text.

The other major change is the division of the book into six sections: history, basic sciences, general anaesthesia, choice of anaesthetic, regional techniques and cardio-respiratory intensive care. This appears to be a new concept but it has been achieved largely by logical reorganisation rather than by the inclusion of new material. The first section on history, while undoubtedly still worthy of inclusion, is woefully short of recent developments. Has there really only been one significant advance since 1971?

The second section, on basic sciences, is subdivided into three parts. The first on physiology is reasonably detailed although the authors deal only with central nervous, autonomic, cardiovascular, respiratory and electrolyte physiology with the notable exceptions of the renal and endocrine systems.

Both pharmacology and physics sections are far too brief to be of much value and really serve to introduce these areas and to advise on further reading. Further reorganisation of basic pharmacological principles such as uptake and distribution of volatile agents, could make this section more worthwhile.

Clinical anaesthesia has again been reorganised and updated, particularly in the light of recent advances in

anaesthetic pharmacology. The chapter on muscle relaxants now includes an extensive section on electromyography and pharmacokinetics, which is a welcome addition. Other additions include a comprehensive page on dental damage(!) and discussion of newer drugs such as calcium antagonists, but not ACE inhibitors. The chapter on hypnosis and electrical anaesthesia has now presumably been consigned to history!

The chapter in Section 4 on medical diseases that influence anaesthesia, has been updated considerably with good results but, as before, the dictionary of rare diseases is irritatingly brief and of use only in the provision of the definitive reference. Two or three lines on each disease with the reference would produce a far more informative contribution. There are some omissions; there is no mention of anaesthesia for microvascular surgery but neuroradiological anaesthesia, particularly for pneumoencephalography, is virtually nonexistent with the advent of CAT and MRI scanning.

Section 5, on regional anaesthesia, remains a particularly valuable part of this book and Section 6, on critical care, also provides a useful introduction. Omissions are inevitable with the frequent advances which occur in critical care: no mention is made of SIMV or pressure support ventilatory modes. The chapters on poisoning and renal and hepatic failure have been omitted, which seems strange since they are hardly irrelevant to current practice.

The references, which represent a valuable part of this book, have been well updated and reduced a little in number without detriment. It is interesting that a review of the first edition cited the lack of references as a criticism! The index, as always, is extremely comprehensive and easy to use. *Synopsis* has rightly become a standard anaesthetic text, particularly for the practising clinical anaesthetist. A volume of this size can never be comprehensive in all areas but in this new format it has certainly become far easier to read and less of a mass of print, although the number of tables and illustrations remains virtually unchanged. This, and its very reasonable price, certainly make the 10th edition a worthwhile addition to the library of all clinicians and departmental libraries.

P.J. SIMPSON

Decision making in anesthesiology

Edited by L.L. BREADY AND R.B. SMITH. Pp. xvii + 281. B.C. Decker Inc., 1987. £41.50.

This book provides a new format of teaching in anaesthesia. One hundred and thirty-five topics are presented in an algorithm or flow-chart format. The relevant features to be found on clinical evaluation are listed and the reader is led through the various choices which are available for clinical management. Possible complications and their management are identified at each step. Clearly, only a very limited amount of information can be included in flow charts of this nature, and more detailed notes and a short list of key references are provided on the page opposite each algorithm.

The book is divided into several sections which deal with the principles of anaesthesia, clinical management of anaesthesia for a variety of surgical specialties, and pre- and postoperative complications. Some topics, for example the management of an unsuspected difficult intubation, are well suited to an algorithm format; the value of this format in others (e.g. respiration) is more dubious. On balance, however, this approach works well, despite an initially confusing number of abbreviations. Most of the flow charts have a clear presentation, aided by the use of bold type for major

steps, and by enclosing important therapeutic interventions in boxes.

It is a little difficult to evaluate the role of the book. The algorithm format is useful for the trainee in that it encourages a logical approach to decision making. However, the style is, of necessity, dogmatic and many of the decisions are not explained. The book will thus be of less value to the new trainee than to the junior anaesthetist who has already studied the subject in some depth. It might be useful for the trainee to refer to these algorithms when presented with an unfamiliar emergency situation but the book is far too large to be carried in the pocket of even the most voluminous white coat.

Inevitably, one does not agree with all of the recommended courses of action and the editors acknowledge that alternative but appropriate techniques may have been omitted. There is considerable duplication of material, since some clinical choices are common to many situations. All but one of the contributors are American and the drug names and description of apparatus may be confusing to the British trainee. A handful of diagrams and one photograph are used to expand the notes that accompany a few of the algorithms. The index is comprehensive.

Despite an initial dislike of the concept of 'anaesthesia by recipe', I found that many of the algorithms summarised efficiently the thought processes of the experienced anaesthetist. The incorporation of a system of priorities would have been a useful addition, although priorities are often determined by the circumstances of an individual patient. Many of the algorithms are very similar to a good draft plan for a written examination answer. Consequently, this book may be useful to trainees revising for examinations, and for teachers, particularly of tutorial groups. There is, in my opinion, too little in the way of explanation to permit its recommendation as a primary source of knowledge for the trainee. However, it would be a popular reference source for the duty anaesthetist if the publishers could be persuaded to produce a pocket-sized version.

A.R. AITKENHEAD

Anesthesia and organ transplantation

Edited by S. GELMAN. Pp. xvi + 254. W.B. Saunders, 1987. £45.00.

The idea of transplantation as a surgical entity is widespread although almost the only link between grafting of various organs is the need for measures to prevent rejection. This may also apply to anaesthesia but the best anaesthetist for the patient who has an organ graft is surely one who is familiar with anaesthesia for the surgery of that organ. Nevertheless, there is a big enough common core of subjects to justify this book.

It consists of a series of chapters by authors from American centres. Six of the twelve are relevant to all recipients. Immunological aspects of graft rejection and immunosuppressive therapy are covered by Rabin and by Shaw and Wood, respectively. The chapter by McKay and Varner on brain death and ethics of organ transplantation relates primarily to practice within the United States, which differs in some respects from that in Britain, for example over the need for electrical and other methods for the diagnosis of brain death. The chapter on organ preservation by Parks and Freeman gives a good review of both theory and current practice. The rather depressing story of infection and organ transplantation is covered by Ho, whose advice is sensible although conventional; selective decontamination of the gastrointestinal tract is not mentioned.

There follow chapters on kidney, heart, heart-lung and

liver grafting, all written by anaesthetists with experience in these areas. The first, by Graybar and Tarpey, starts with the anatomy and physiology, followed by history and then descriptions of donor nephrectomy (in both live and cadaveric donors), surgical technique, anaesthetic management (of living and cadaveric donors as well as of the recipients) and the pathophysiology of renal failure, and ends with the results. The second, by Wyner and Finch, also starts with a history and continues with the physiology of the denervated heart and the surgical and anaesthetic management of both donors and recipients. The last, by Kang and Gelman, begins with the anatomy and physiology of the liver and biliary system and then discusses pathophysiology, the history of the procedure, selection and management of donors and the operation in recipients, followed by anaesthetic management. It concludes with post-operative management and the results.

A chapter entitled 'Blood transplantation—blood transfusion' by Ebert aptly reminds us that patients who have major transplantations, particularly of the liver, may receive complete exchanges of their blood volumes. He discusses storage of red cells, depletion of 2,3-DPG, citrate intoxication, hyperkalaemia, hypothermia, micro-aggregates and leaching of plasticiser from PVC bags. Auto-transfusion, infective hazards of blood transfusion and its immunological effects on graft rejection are also discussed. This chapter is surely important enough to have been included in the earlier section of the book.

Lastly, there are two chapters on reimplantation of severed limbs and skin transplantation which deal with organs and tissues not subject to rejection. The inclusion of these two titles seems idiosyncratic; why not a chapter on the use of teflon arterial grafts? Perhaps most disappointing is the absence of chapters on bone marrow transplantation and on corneal grafting. Nevertheless, this book is well presented and written and is a valuable source of information on the subjects which are covered. It should be read

by anaesthetists engaged in organ transplantation and certainly deserves a place on the departmental bookshelf.

J.V. FARMAN

Books received

We wish to thank all those publishers who have sent in publications, some or all of which may be reviewed in future issues of *Anaesthesia*.

Manual of anaesthesia in cancer care

W.S. HOWLAND, S.M. ROONEY AND P.L. GOLDINER. Pp. 321. Churchill Livingstone, 1986. £22.00.

Anaesthesia and intensive care for the neurosurgical patient

S.M. WILLATTS AND F.J.M. WALTERS. Pp. 337. Blackwells, 1986. £35.00.

Monitoring cerebral function. Long-term monitoring of EEG and evoked potentials

P.F. PRIOR AND D.E. MAYNARD. Pp. 441. Elsevier, 1986. £95.

Databook of anaesthesia and critical care medicine, 4th edn

P.A. FOSTER AND J.A. ROELOFSE. Pp. x + 204. Springer-Verlag, 1987. DM 42.00.

1987 Year book of anaesthesia

Edited by R.D. MILLER, R.R. KIRBY, G.W. OSTHEIMER, M.F. ROIZEN AND R.K. STOELTING. Year Book Medical Publishers, Inc., 1987. £37.50.

Advances in trauma, Vol. 2

Edited by K.I. MAULL, H.C. CLEVELAND, G.O. STRAUCH AND C.C. WOLFERTH. Year Book Medical Publishers, Inc., 1987. £45.00.

Current European anesthesiology, Vol. 3

Edited by R.M. JONES, H. BERGMANN, J. LASSNER, J.C. OTTENI AND D. THOMSON. Wiley, 1987.

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for October 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

- Patients with irritable bowel syndrome have greater pain tolerance than normal subjects. COOK IJ, VAN EEDEN A, COLLINS SM. *Gastroenterology* 1987; **93**: 727.
- Effect of systemic acid-base balance on ileal secretion. GOLDFARB DS, INGRASSIA PM, CHARNEY AN. *American Journal of Physiology* 1987; **253**: G330.
- Prevention of bowel ischaemia following surgery to the abdominal aorta: a review. KLOMPJE J. *Journal of the Royal Society of Medicine* 1987; **80**: 574.
- Sigmoid intramural pH for prediction of ischemic colitis during aortic surgery: comparison with risk factors and inferior mesenteric artery stump pressures. SCHIEDLER MG, BRUCE SC *et al.* *Archives of Surgery* 1987; **122**: 881.
- Study on glucocorticoid receptors during intestinal ischemia shock and septic shock. ZONGHAI H, HAN G, RENBAO X. *Circulatory Shock* 1987; **23**: 27.

Pharmacology

Adrenergic drugs and their antagonists

- Peripheral vascular effects of beta-adrenoceptor blockade: comparison of two agents. COOKE ED, MALTZ MB *et al.* *British Journal of Clinical Pharmacology* 1987; **24**: 359.
- Beta-adrenergic relaxation of smooth muscle: differences between cells and tissues. SCHEID CR. *American Journal of Physiology* 1987; **253**: C369.
- Mechanism of action of indirectly acting sympathomimetic amines. TRENDLENBURG U, LANGELOH A, BONISCH H. *Blood Vessels* 1987; **24**: 261.

Anaesthetic agents

- Comparison of the respiratory depressant effects of halothane and isoflurane in routine surgery. ALAGESAN K, NUNN JF *et al.* *British Journal of Anaesthesia* 1987; **59**: 1070.
- Ethanol and nitrous oxide produce withdrawal induced convulsions by similar mechanisms in mice. BELKNAP JK, LAURSEN SE, CRABBE JC. *Life Sciences* 1987; **41**: 2033.
- Pharmacokinetics of propofol in female patients—studies using single bolus injections. COCKSHOTT ID, BRIGGS LP. *British Journal of Anaesthesia* 1987; **59**: 1103.
- Effect of etomidate on adrenal function in rats. HAMPL R, BICIKOVA M *et al.* *Endocrinologia Experimentalis* 1987; **21**: 229.
- Trichloroethylene inhibits uptake of H-3-5-hydroxytryptamine but not uptake of H-3-zimeldine or H-3-propranolol in isolated perfused rat lungs. HEDE AR, BERGLUND BG, POST C. *Pharmacology and Toxicology* 1987; **61**: 138.
- The carcinogenicity of trichloroethylene and its metabolites, trichloroacetic acid and dichloroacetic acid, in mouse liver. HERREN-FREUND SL, PEREIRA M *et al.* *Toxicology and Applied Pharmacology* 1987; **90**: 183.
- Anaesthetic properties of pregnanolone emulsion. A comparison with alphaxolone/alphadolone, propofol, thiopentone and midazolam in a rat model. HOGSKILDE S, WAGNER J *et al.* *Journal of Pathology* 1987; **153**: 1045.

- Pulmonary arterial pressure-flow plots in dogs: effects of isoflurane and nitroprusside. NAEIJE R, LEJEUNE P *et al.* *Journal of Applied Physiology* 1987; **63**: 969.

Analgesic agents

- Explanation for potency of repeated oral doses of morphine? HANKS GW, HOSKIN PJ *et al.* *Lancet* 1987; **2**: 723.
- Arrhythmogenic, antiarrhythmic and inotropic properties of opioids. Effects of piritramide, pethidine and morphine compared on heart muscle isolated from rats. HELGESEN KG, REFSUM H. *Pharmacology* 1987; **35**: 121.
- Morphine and fentanyl hypnotic interaction with thiopental. KISSIN I, MASON JO, BRADLEY EL. *Anesthesiology* 1987; **67**: 331.
- Naloxone inhibits the centrally-mediated hypotensive actions of BHT-933 (azepevole). TACKETT RL, LASKEY R. *Life Sciences* 1987; **41**: 2063.

Muscle relaxants

- The effects of vecuronium on intra-ocular pressure. MIRAKHUR RK, SHEPHERD WFI *et al.* *Anaesthesia* 1987; **42**: 944.
- Effect of an intubating dose of succinylcholine and atracurium on the diaphragm and the adductor pollicis muscle in humans. PANSARD J, CHAUVIN M *et al.* *Anesthesiology* 1987; **67**: 326.
- Treatment of myasthenia gravis—an audit. SIMPSON JA, THOMAIDES T. *Quarterly Journal of Medicine* 1987; **64**: 693.
- Suxamethonium in myasthenia gravis. WAINWRIGHT AP, BRODRICK PM. *Anaesthesia* 1987; **42**: 950.

Other drugs

- Dependence of tonic tension on extracellular calcium in rat extra-ocular muscle. CHIARANDINI DJ, JACOBY J. *American Journal of Physiology* 1987; **253** (No. 3, Part 1): C375.
- Ethanol metabolism. CRABB DW, BOSRON WF, LI TK. *Pharmacology and Therapeutics* 1987; **34**: 59.
- Circulatory and respiratory effects of infused adenosine in conscious man. FULLER RW, MAXWELL DL *et al.* *British Journal of Clinical Pharmacology* 1987; **24**: 309.
- Heparin modulates human intestinal smooth muscle cell proliferation, protein synthesis and lattice contraction. GRAHAM MF, DRUCKER DEM *et al.* *Gastroenterology* 1987; **93**: 801.
- Characterisation of theophylline metabolism in human liver microsomes. ROBSON RA, MATTHEWS AP *et al.* *British Journal of Clinical Pharmacology* 1987; **24**: 293.
- Theophylline disposition during acute and chronic hypoxia in the conscious dog. SAUNIER C, DU SOUCH P *et al.* *Research Communications in Chemical Pathology and Pharmacology* 1987; **57**: 291.

Apparatus

- Clinical use of peripheral nerve stimulators in anaesthesia. HUDES E, LEE KC. *Canadian Journal of Anaesthesia* 1987; **34**: 525.
- Accurate, automated, continuously displayed pulmonary artery pressure measurement. MITCHELL MM, MEATHE EA *et al.* *Anesthesiology* 1987; **67**: 294.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

The flow-pressure characteristics of compressors used for inhalation therapy. NEWMAN SP, PELLOW PGD, CLARKE SW. *European Journal of Respiratory Disease* 1987; 71: 122.

Complications

Pretreatment with corticosteroids to alleviate reactions to intravenous contrast material. LASSER EC, BERRY CC *et al.* *New England Journal of Medicine* 1987; 317: 845.

Critical illness polyneuropathy. A complication of sepsis and multiple organ failure. ZOCHODNE DW, BOLTON CF *et al.* *Brain* 1987; 110: 819.

General anaesthetic procedures

One lung anaesthesia. Cardiovascular and respiratory function compared during conventional ventilation and high frequency jet ventilation. JENKINS J, CAMERON EWJ *et al.* *Anaesthesia* 1987; 42: 938.

Propofol infusion for sedation in intensive care. NEWMAN LH, McDONALD JC *et al.* *Anaesthesia* 1987; 42: 929.

Preoperative pulmonary blood flow and one-lung anaesthesia. NOMOTO Y. *Canadian Journal of Anaesthesia* 1987; 34: 447.

Palliative intubation of the tracheobronchial tree. ORLOWSKI TM. *Journal of Thoracic and Cardiovascular Surgery* 1987; 94: 343.

Electroconvulsive therapy—1987. SELVIN BL. *Anesthesiology* 1987; 67: 367.

General interest

Current concepts: lymphokines. DINARELLO CA, MIER JW. *New England Journal of Medicine* 1987; 317: 940.

Impaired water excretion and elevated plasma vasopressin in patients with alcohol withdrawal symptoms. EMSLEY RA, POTGIETER A *et al.* *Quarterly Journal of Medicine* 1987; 64: 671.

Cerebral auscultation—origin of a forgotten art. GORELICK PB, SULLIVAN M, LANSKY L. *Neurology* 1987; 37: 1523.

Hemostatic evaluation of patients undergoing liver transplantation. OWEN CA, RETTKE SR *et al.* *Mayo Clinic Proceedings* 1987; 62: 761.

Some aspects of neuroendocrine pathology. POLAK JM, BLOOM SR. *Journal of Clinical Pathology* 1987; 40: 1024.

Efficiency of intensive care. POLLACK MM, GETSON PR *et al.* *Journal of the American Medical Association* 1987; 258: 1481.

Diagnosis of acute pancreatitis: a proposed sequence of biochemical investigations. THOMPSON JH, OBEKPA PO *et al.* *Scandinavian Journal of Gastroenterology* 1987; 22: 719.

Local analgesia

Serum lidocaine concentrations following application to the oropharynx: effects of cimetidine. PARISH RC, GOTZ VP *et al.* *Therapeutic Drug Monitoring* 1987; 9: 292.

Freeze fracture analysis of muscle plasma membrane in bupivacaine HCl-induced degeneration and regeneration. YOSHIMURA T, SCHOTLAND DL. *Journal of Neuropathology and Experimental Neurology* 1987; 46: 522.

Spinal and epidural analgesia

Continuous epidural anesthesia and postoperative epidural narcotics in vascular surgery. RAGGI R, DARDIK H, MAURO AL. *American Journal of Surgery* 1987; 154: 192.

Spinal opioids

The effect of endogenous opioids on blood pressure during stress. NORDIN M, MORAT P, ZAINORA M. *Clinical and Experimental Pharmacology and Physiology* 1987; 14: 303.

Antinociceptive effects in mice after intrathecal injection of a substance P receptor antagonist, Spantide: lack of 'neurotoxic' action. POST C, FREEDMAN J *et al.* *Regulatory Peptides* 1987; 18: 243.

Obstetric anaesthesia and analgesia

Epidural fentanyl/bupivacaine mixture for obstetric analgesia. COHEN SE, TAN S *et al.* *Anesthesiology* 1987; 67: 403.

A classification of hypertension in pregnancy based on doppler velocimetry. DUCEY J, SCHULMAN H *et al.* *American Journal of Obstetrics and Gynecology* 1987; 157: 680.

Effect of pre-eclampsia on plasma cholinesterase activity. KAMBAM JR, MOUTON S *et al.* *Canadian Journal of Anaesthesia* 1987; 34: 509.

Gestational diabetes: insulin requirements in pregnancy. LANGER O, ANYAEBUNAM A *et al.* *American Journal of Obstetrics and Gynecology* 1987; 157: 669.

Hypertension in pregnancy. MARIKRANZ P, LINDHEIMER MD. *Medical Clinics of North America* 1987; 71: 1031.

Cocaine use during pregnancy: adverse perinatal outcome. MACGREGOR SN, KETH LG *et al.* *American Journal of Obstetrics and Gynecology* 1987; 157: 686.

Drug metabolism in pregnancy, infancy and childhood. PERUCCA E. *Pharmacology and Therapeutics* 1987; 34: 129.

Paediatric anaesthesia and intensive care

Comparison of respiratory inductive plethysmograph and thoracic impedance for apnea monitoring. BROUILLETTE RT, MORROW AS *et al.* *Journal of Pediatrics* 1987; 111: 377.

The central venous anatomy in infants. COBB LM, VINOCUR CD *et al.* *Surgery, Gynecology and Obstetrics* 1987; 165: 239.

Prolonged intubation of neonates. DANKLE SK, SCHULLER DE, MCCLEAD RE. *Archives of Otolaryngology—Head and Neck Surgery* 1987; 113: 841.

Postnatal changes in colloid osmotic pressure in premature infants. EKBLAD H. *Gynecologic and Obstetric Investigation* 1987; 24: 95.

Correlation between function of the pituitary-thyroid axis and metabolism of catecholamines by the fetus at delivery. FUKUDA S. *Clinical Endocrinology* 1987; 27: 331.

Synchronous respiration: which ventilator rate is best? GREENOUGH A, GREENALL F, GAMSU H. *Acta Paediatrica Scandinavica* 1987; 76: 713.

Comparison of different rates of artificial ventilation in preterm neonates with respiratory distress syndrome. GREENOUGH A, POOL A *et al.* *Acta Paediatrica Scandinavica* 1987; 76: 706.

Extracorporeal membrane oxygenation following repair of congenital diaphragmatic hernias. LANGHAM MR, KRUMMEL TM *et al.* *Annals of Thoracic Surgery* 1987; 44: 247.

The minimum alveolar concentration (MAC) of isoflurane in preterm neonates. LEDEZ KM, LERMAN J. *Anesthesiology* 1987; 67: 301.

Severe neonatal respiratory distress syndrome treated with the isolated phospholipid fraction of natural surfactant. NOACK G, BERGGREN P *et al.* *Acta Paediatrica Scandinavica* 1987; 76: 697.

Familial occurrence of sudden infant death syndrome and apnea of infancy. OREN J, KELLY DH, SHANNON DC. *Pediatrics* 1987; 80: 355.

Fulminant hepatic failure. RUSSEL GJ, FITZGERALD JF, CLARK JH. *Journal of Pediatrics* 1987; 111: 313.

Effect of anaemia on fetal acid-base status. SOOTHILL PW, NICOLAIDES KH, RODECK CH. *British Journal of Obstetrics and Gynaecology* 1987; 94: 880.

Atrial natriuretic peptide and other vasoactive hormones during treatment of severe diabetic ketoacidosis in children. TULASSAY T, RASCHER W *et al.* *Journal of Pediatrics* 1987; 111: 329.

Prediction of arterial blood pressure in the premature neonate using the oscillometric method. WAREHAM JA, HAUGH LD *et al.* *American Journal of Diseases of Children* 1987; 141: 1108.

Analgesia and anesthesia in neonates. YASTER M. *Journal of Pediatrics* 1987; 111: 394.

Cardiovascular system

Physiology

Research review. The applied anatomy of the arterial blood supply to the heart in man. ALLWORK SP. *Journal of Anatomy* 1987; 153: 1.

Total body electrolyte composition in patients with heart failure: a comparison with normal subjects and patients with untreated hypertension. CLELAND JGF, DARGIE HJ *et al.* *British Heart Journal* 1987; 58: 230.

Baroreceptor function in man following peripheral alpha-1-adrenoceptor and alpha-2-adrenoceptor stimulation. DEERING AH, RIDDELL JG *et al.* *European Journal of Clinical Pharmacology* 1987; 33: 41.

- Cardiac involvement in essential hypertension: prevalence, pathophysiology, and prognostic implications. DEVEREUX RB. *Medical Clinics of North America* 1987; **71**: 813.
- Mechanism of increased alpha adrenergic vasoconstriction in human essential hypertension. EGAN B, PANIS R *et al.* *Journal of Clinical Investigation* 1987; **80**: 812.
- Psychological stress and silent myocardial ischemia. FREEMAN LJ, NIXON PGF *et al.* *American Heart Journal* 1987; **114**: 477.
- Atrial natriuretic factor—a historic perspective. FRIED T. *American Journal of the Medical Sciences* 1987; **294**: 134.
- Nervous control of glycogenolysis and blood flow in arterially and portally perfused liver. GARDEMANN A, STRULIK H, JUNGGERMANN K. *American Journal of Physiology* 1987; **253**: E283.
- Alterations of electrolytes in serum and erythrocytes after myocardial infarction. GUNTHER IH, BERTSCHAT T *et al.* *Magnesium* 1987; **6**: 192.
- Congestive cardiac failure: central role of the arterial blood pressure. HARRIS P. *British Heart Journal* 1987; **58**: 190.
- The pathology of the early and late stages of primary pulmonary hypertension. HEATH D, SMITH P *et al.* *British Heart Journal* 1987; **58**: 204.
- Continuous monitoring of blood volume changes in humans. HINGHOFFER-SZALKAY H, GREENLEAF JE. *Journal of Applied Physiology* 1987; **63**: 1003.
- Sickle-cell trait as a risk factor for sudden death in physical training. KARK JA, POSEY DM *et al.* *New England Journal of Medicine* 1987; **317**: 781.
- Hemorrhagic shock prevents lung microvascular permeability and hypoxemia associated with complement activation in the awake sheep. KRAUSZ MM, SHILO L *et al.* *Circulatory Shock* 1987; **23**: 7.
- Autonomic function in mitral valve prolapse. LEADING ARTICLE. *Lancet* 1987; **2**: 773.
- Pathology of the human heart in drowning. LUNT DWR, ROSE AG. *Archives of Pathology and Laboratory Medicine* 1987; **111**: 939.
- Role of atrial natriuretic polypeptides for exaggerated natriuresis in essential hypertension. MATSUBARA H *et al.* *American Journal of Cardiology* 1987; **60**: 708.
- Dual effects of norepinephrine and mechanisms of baroreceptor stimulation. MUNCH PA, THOREN PN, BROWN AM. *Circulation Research* 1987; **61**: 409.
- Ventricular arrhythmias in patients with hypertensive left ventricular hypertrophy. MCLENACHAN JM, HENDERSON E *et al.* *New England Journal of Medicine* 1987; **317**: 787.
- Role of cardiac parasympathetic dysfunction in atrial natriuretic peptide response to volume changes in patients with chronic renal failure. PRUSZCZYNSKI W, VIRON B *et al.* *Mineral and Electrolyte Metabolism* 1987; **13**: 333.
- Silent myocardial ischemia. I. Pathophysiology, frequency of occurrence, and approaches toward detection. ROZANSKI A, BERMAN DS. *American Heart Journal* 1987; **114**: 615.
- Molecular approaches to the study of atrial natriuretic factor—review. SEIDMAN CE, BLOCH KD. *American Journal of Medical Science* 1987; **294**: 144.
- Coronary flow reserve and diastolic dysfunction in hypertrophic cardiomyopathy. TENCATE FJ, SERRUYS PW. *International Journal of Cardiology* 1987; **17**: 25.
- Cardiovascular effects of serotonin. VANHOUTTE PM. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 3): S8.
- Treatment and medication**
- Comparison in young and elderly patients of pharmacodynamics and disposition of labetalol in systemic hypertension. ABERNETHY DR, SCHWARTZ JB *et al.* *American Journal of Cardiology* 1987; **60**: 697.
- Effect of ibuprofen on the course of canine endotoxin shock. BECK RR, ABEL FL. *Circulatory Shock* 1987; **23**: 59.
- Free radicals and cardioplegia: allopurinol and oxypurinol reduce myocardial injury following ischemic arrest. CHAMBERS DJ, BRAIMBRIDGE MV, HEARSE DJ. *Annals of Thoracic Surgery* 1987; **44**: 291.
- Perforated peptic ulcer—a complication in acute salicylate intoxication. CHRISTENSEN LA, SCHMIDT EB. *Acta Medica Scandinavica* 1987; **222**: 191.
- Resuscitation fluid composition and myocardial performance during burn shock. CONAHAN ST, DUPRE A *et al.* *Circulatory Shock* 1987; **23**: 37.
- Reduction of stress/catecholamine-induced cardiac necrosis by beta-1-selective blockade. CRUICKSHANK JM, NEIL-DWYER G *et al.* *Lancet* 1987; **2**: 585.
- Effects of training in cardiopulmonary resuscitation on competence and patient outcome. CURRY L, GASS D. *Canadian Medical Association Journal* 1987; **137**: 491.
- Prognosis and clinical follow-up of patients resuscitated from out of hospital cardiac arrest. JAKOBSSON J, NYQUIST O *et al.* *Acta Medica Scandinavica* 1987; **222**: 123.
- Nonpharmacologic therapy of hypertension. KAPLAN NM. *Medical Clinics of North America* 1987; **71**: 921.
- Possible deleterious hemodynamic effect of nifedipine on portal hypertension in patients with cirrhosis. KOSHY A, HADENGUE A *et al.* *Clinical Pharmacology and Therapeutics* 1987; **42**: 295.
- Electrophysiologic study in the management of cardiac arrest survivors: a critical review. LO Y-SA, NGUYEN KPV. *American Heart Journal* 1987; **114**: 596.
- Mixed venous oxygen saturation as a predictor of cardiac output in the postoperative cardiac surgical patient. MAGILLIGAN DJ, REASDAL R *et al.* *Annals of Thoracic Surgery* 1987; **40**: 260.
- Acute hemodynamic and neurohumoral effects of pindolol: an antagonist with high intrinsic sympathomimetic activity in patients with dilated cardiomyopathy. MAJID PA, NIZNICK J *et al.* *Journal of Cardiovascular Pharmacology* 1987; **10**: 309.
- Disturbances of sleep and wakefulness associated with the use of antihypertensive agents. MONTI JM. *Life Sciences* 1987; **41**: 1979.
- Diuretics in the management of hypertension. MOSER M. *Medical Clinics of North America* 1987; **71**: 930.
- Treatment of systemic hypertension. MACGREGOR GA. *American Journal of Cardiology* 1987; **60**: 9E.
- Factors influencing treatment of hypertension. ROBERTSON JIS. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 2): S76.
- A new method of rapid fluid resuscitation during thoracotomy performed in the emergency room. SAMELSON SL, ROBIN AP *et al.* *Surgery, Gynecology and Obstetrics* 1987; **165**: 175.
- Review of clinical studies of thrombolytic agents in acute myocardial infarction. SCHREIBER T. *American Journal of Medicine* 1987; **83** (No. 2A): 20.
- Changes in lignocaine disposition during long-term infusion in patients with acute ventricular arrhythmias. THOMSON AH, KELMAN AW *et al.* *Therapeutic Drug Monitoring* 1987; **9**: 283.
- Nifedipine and metoprolol in unstable angina: findings from the Holland interuniversity nifedipine/metoprolol trial. TUSSEN JGP, LUBSEN J. *Journal of Cardiovascular Pharmacology* 1987; **10** (Suppl. 2): S15.
- Continuous positive airway pressure and supplemental oxygen in the treatment of cardiogenic pulmonary edema. VAISANEN IT, RASANEN J. *Chest* 1987; **92**: 481.
- Cardiac failure in the elderly. WEBB SC, IMPALLOMENI MG. *Quarterly Journal of Medicine* 1987; **64**: 641.
- Respiration**
- Physiology**
- Ozone exposure alters tracheobronchial mucociliary function in humans. FOSTER WM, COSTA DL, LANGENBACK EG. *Journal of Applied Physiology* 1987; **63**: 996.
- Arterial oxygen saturation during bronchography via the fibreoptic bronchoscope. GOLDMAN JM, CURRIE DC *et al.* *Thorax* 1987; **42**: 694.
- Phasic changes in upper airway impedance. HAFFER CE, STROHL KP, FOUKE JM. *Respiration Physiology* 1987; **70**: 13.
- Airway anaesthesia and the cough reflex. KARLSSON JA. *Clinical Respiratory Physiology* 1987; **23** (Suppl.): 29S.
- Obstructive sleep apnoea and lower airways obstruction. LEADING ARTICLE. *Lancet* 1987; **2**: 774.
- Mechanisms of the inhibition of cytochrome P-450-mediated drug oxidation by therapeutic agents. MURRAY M. *Drug Metabolism Reviews* 1987; **18**: 55.
- Late asthmatic responses. OBYRNE PM, DOLOVICH J, HARGREAVE FE. *American Review of Respiratory Disease* 1987; **135**: 740.
- Effect of dynamic airway compression on breathing pattern and respiratory sensation in severe chronic obstructive pulmonary disease. O'DONNELL DE, SANI R *et al.* *American Review of Respiratory Disease* 1987; **135**: 912.
- Effect of theophylline on respiratory neuromuscular drive. OKUBO S, KONNO K *et al.* *European Journal of Clinical Pharmacology* 1987; **33**: 85.

- Pulmonary edema with smoke inhalation, undetected by indicator-dilution technique. PRIEN T, TRABE LD *et al. Journal of Applied Physiology* 1987; **63**: 907.
- Ventilatory effects of stimulation of phrenic afferents. ROAD JD, WEST NH, VAN VLIET BN. *Journal of Applied Physiology* 1987; **63**: 1063.
- Hyperoxic-induced hypercapnia in stable chronic obstructive pulmonary disease. SASSOON CSH, HASSELL KT, MAHUTTE CK. *American Review of Respiratory Disease* 1987; **135**: 907.
- Effects of hyperthermia and hypothermia on oxygen extraction by tissues during hypovolemia. SCHUMACKER PT, ROWLAND J *et al. Journal of Applied Physiology* 1987; **63**: 1246.
- Fluid balance and the adult respiratory distress syndrome. SEIDENFELD JJ, PRIHODA TJ *et al. American Review of Respiratory Disease* 1987; **135**: 924.
- Absence of regional differences in the size and oxidative capacity of diaphragm muscle fibres. SIECK GC, SACKS RD, BIANCO CE. *Journal of Applied Physiology* 1987; **63**: 1076.
- Airway smooth muscle. STEPHENS NL. *American Review of Respiratory Disease* 1987; **135**: 960.
- Effect of acute diaphragm paralysis on ventilation in awake and sleeping dogs. STRADLING JR, KOZAR LF *et al. American Review of Respiratory Disease* 1987; **135**: 633.
- Ventilation-perfusion inequality in chronic asthma. WAGNER PD, HEDENSTIERNA G, BYLIN G. *American Review of Respiratory Disease* 1987; **135**: 605.
- Respiratory disorders of sleep—pathophysiology, clinical implications and therapeutic approaches. WEIL JV, CHERNIACK NS *et al. American Review of Respiratory Disease* 1987; **135**: 755.

Treatment and medication

- Noninvasive tests for responsiveness of pulmonary hypertension to oxygen—prediction of survival in chronic obstructive lung disease and cor pulmonale. ASHUTOSH K, DUNSKY M. *Chest* 1987; **92**: 393.
- Effect of PEEP on the arterial minus end-tidal carbon dioxide gradient. FERNANDEZ R, BENITO S *et al. Chest* 1987; **92**: 451.
- Home oxygen therapy. PETTY TL. *Mayo Clinic Proceedings* 1987; **62**: 841.
- Use of steroids and a long-acting vasoconstrictor in the treatment of postintubation croup. POSTMA DS, PRAZMA J *et al. Archives of Otolaryngology—Head and Neck Surgery* 1987; **113**: 844.

Central nervous system

Physiology

- Minireview: axonal regeneration, growth factors and neuropeptides. DEKKER A, GISPEN WH, DE WIED D. *Life Sciences* 1987; **41**: 1667.
- Biochemistry, anatomy and pharmacology of GABA neurons. FONNUM F. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 173.
- The effect of extradural blockade upon glucose and urea kinetics in surgical patients. GALLER L, HOLDAWAY IM, HOLDAWAY CM. *Surgery, Gynecology and Obstetrics* 1987; **165**: 260.
- Pressure-volume index as a function of cerebral perfusion pressure. 1. The effects of cerebral perfusion changes and anesthesia. GRAY WJ, ROSNER MJ. *Journal of Neurosurgery* 1987; **67**: 369.
- Pressure-volume index as a function of cerebral perfusion pressure. 2. The effects of low cerebral perfusion pressure and autoregulation. GRAY WJ, ROSNER MJ. *Journal of Neurosurgery* 1987; **67**: 377.
- Snoring, nocturnal hypoxemia and the effect of oxygen inhalation. HELLARD DW, CICALA MJ. *Chest* 1987; **92**: 411.
- Changes in inspiratory muscle electrical activity and upper airway resistance during periodic breathing induced by hypoxia during sleep. HUDGEL DW, CHAPMAN KR. *American Review of Respiratory Disease* 1987; **135**: 899.
- GABA and affective disorders. LLOYD KG, MORSELLIE PL, BARTHOLOMI G. *Medical Biology* 1987; **65**: 159.
- The concept of coupling blood flow to brain function: revision required? LOU HC, EDVINSSON L, MACKENZIE ET. *Annals of Neurology* 1987; **22**: 289.
- Hypothalamic dopaminergic neuronal systems. MOORE KE. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 127.

- Measurement of total circulating blood volume following sub-arachnoid haemorrhage—methodological aspects. NELSON RJ, ROBERTS J *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1987; **50**: 1130.
- Electron microscopy of central catecholamine systems. PICKEL VM, MILNER TA. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 49.
- Sleep and affective disorders. REYNOLDS CF, GILLIN JC, KUPFER DJ. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 647.
- Neurochemistry of midbrain dopamine systems. ROTH RH, WOLF ME, DEUTCH AY. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 81.
- GABA-benzodiazepine receptor complex and drug actions. SAANO V. *Medical Biology* 1987; **65**: 167.
- Effect of hypocapnia on cerebral oxygen metabolism and blood flow in ischemic cerebrovascular disorders. TSUDA Y, KIMURA K *et al. European Neurology* 1987; **27**: 155.
- Pathogenesis of hepatic encephalopathy. ZIEVE L. *Metabolic Brain Disease* 1987; **2**: 147.

Treatment and medication

- Reduced response of cerebral blood flow to hypercapnia: restoration by extracranial-intracranial bypass. BISHOP CCR, BURNAND KG *et al. British Journal of Surgery* 1987; **74**: 802.
- Reversibility of alcohol-related brain damage: clinical and experimental observations. CARLEN PL, WILKINSON DA. *Acta Medica Scandinavica* 1987; (717 Suppl.): 19.
- Is there a therapeutic role for osmotic breaching of blood-brain barrier? FISHMAN RA. *Annals of Neurology* 1987; **22**: 298.
- Effect of gradual withdrawal on the rebound sleep disorder after discontinuation of triazolam. GREENBLATT DJ, HARMATZ JS *et al. New England Journal of Medicine* 1987; **317**: 722.
- Brain damage in alcoholism: current concepts. LISHMAN WA, JACOBSON RR, ACKER C. *Acta Medica Scandinavica* 1987; (717 Suppl.): 5.
- Upper-airway surgery for treating obstructive sleep apnea. SCHOEN SL, ANAND VK *et al. Archives of Otolaryngology—Head and Neck Surgery* 1987; **113**: 850.

Endocrine and metabolic

Physiology

- Oxytocin and vasopressin: photoaffinity labeling of neurophysins, secretory granule hormone-binding proteins. ABERCROMBIE DM, CHAIKEN IM. *Pharmacology and Therapeutics* 1987; **33**: 209.
- The hypothalamic-pituitary-thyroid axis in affective disorders. BERGER PA, NEMEROFF CB. In: MELTZER HY, ed. *Psychopharmacology. The third generation of progress*. New York: Raven Press, 1987: 637.
- Clinical aspects of endocrine hypertension. BRAVO EL. *Medical Clinics of North America* 1987; **71**: 907.
- Diabetes mellitus as a hypercoagulable state: its relationship with fibrin fragments and vascular damage. FRADE LJG, DE LA CALLE H *et al. Thrombosis Research* 1987; **47**: 533.
- Interaction of vasopressin, angiotensin and alpha-adrenergic system in sodium depletion in the rat. JOVER BF, McGRATH BP. *Clinical and Experimental Pharmacology and Physiology* 1987; **14**: 181.
- Adenosine: emerging role as an immunomodifying agent. KAMMER GM. *Journal of Laboratory and Clinical Medicine* 1987; **110**: 255.
- Shock-induced modulation of lymphocyte reactivity: suppression, habituation, and recovery. LYSLE DT, LYTE M *et al. Life Sciences* 1987; **41**: 1805.
- Aminergic regulation of neuroendocrinological functions—theoretical background and some clinical examples. MANNISTO PT. *Medical Biology* 1987; **65**: 121.
- Changes in plasma renin, insulin, aldosterone and arginine vasopressin during plasmapheresis. RAINFOY M, PRUSZCZYNSKI W *et al. Clinical Science* 1987; **73**: 337.
- The renin-angiotensin systems. RE RN. *Medical Clinics of North America* 1987; **71**: 877.
- Hemodynamic alterations in long term insulin dependent diabetic patients with overt nephropathy: role of blood hyperviscosity and plasma protein changes. SOLERTE SB, FIORAVANTI M. *Clinical Nephrology* 1987; **28**: 138.

Renal impairment following biliary tract surgery. THOMPSON JN, EDWARDS WH *et al. British Journal of Surgery* 1987; **74**: 843.

Metabolic control of kidney hemodynamics in normal and insulin-dependent diabetic subjects: effects of acetoacetic, lactic, and acetic acids. TREVISAN R, NOSADINI R *et al. Diabetes* 1987; **36**: 1073.

Effects of fentanyl on vasopressin secretion in human subjects. WEISKOPF RB, REID IA *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; **242**: 970.

Increased levels of plasma renin, aldosterone, catecholamines and vasopressin in chronic ambulatory peritoneal dialysis (CAPD) patients. ZABETAKIS PM, KUMAR DN *et al. Clinical Nephrology* 1987; **28**: 147.

Treatment and medication

Intravenously administered frusemide increases glomerular permeability. ALA-HOUHALA I, VAPAATALO H, PASTERNAK A. *Clinical Science* 1987; **73**: 365.

Fructose prevents hypoxic cell death in liver. ANUNDI I, KING J *et al. American Journal of Physiology* 1987; **253**: G390.

The role of opiate, dopaminergic and adrenergic systems in the hypothalamo-pituitary dysfunction in obesity. BARANOWSKA B, SINGH SP *et al. Acta Endocrinologica* 1987; **116**: 221.

Clopamide: plasma concentrations and diuretic effect in humans. MCNEIL JJ, CONWAY EL *et al. Clinical Pharmacology and Therapeutics* 1987; **42**: 299.

Cellular calcium in ischemic acute renal failure—role of calcium entry blockers. SCHRIER RW, ARNOLD PE *et al. Kidney International* 1987; **32**: 313.

Drug therapy: the use of ketoconazole as an inhibitor of steroid production. SONINO N. *New England Journal of Medicine* 1987; **317**: 812.

A study on furosemide disposition in man. ZHU J, KOIZUMI T. *Journal of Pharmacobio-Dynamics* 1987; **10**: 370.

The diuretic effect of furosemide in relation to its disposition in man. ZHU J, KOIZUMI T. *Journal of Pharmacobio-Dynamics* 1987; **10**: 377.

Pain

Treatment and medication

Control of postoperative pain—nonnarcotic and narcotic alternatives and their effect on pulmonary function. COLEMAN DL. *Chest* 1987; **92**: 520.

A comparison of nalbuphine and meperidine in treatment of postoperative pain. FORSTER K, GORDON R, HEW E. *Canadian Journal of Anaesthesia* 1987; **34**: 462.

Diclofenac compared with narcotic analgesic in the treatment of biliary pain. LUNDSTAM S, IVARSSON L *et al. Current Therapeutic Research* 1987; **42**: 395.

Pain following periodontal surgery: treatment with a nonnarcotic analgesic compared with two codeine combinations. SCOREN RD, CORN H *et al. Current Therapeutic Research* 1987; **42**: 463.

Meptazinol for postoperative pain relief in man: a comparison of extradural and IM administration. VERBORGH C, VANDERAUWERA D, CAMU F. *British Journal of Anaesthesia* 1987; **59**: 1134.

Other

Physiology

Middle-ear pressure under basal conditions. HERGILS L, MAGNUSON B. *Archives of Otolaryngology—Head and Neck Surgery* 1987; **113**: 829.

Treatment and medication

General principles of antimicrobial therapy. WILKOWSKIE CJ, HERMANS PE. *Mayo Clinic Proceedings* 1987; **62**: 789.

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A number of incidents have occurred in which the above equipment failed to operate and ventilation of the patients' lungs ceased. Springs and rubber tubing should be replaced each year. This recommendation applies to ventilator Model numbers MN2, MP2, MP3, BM2, M4 and the Blease Brompton.

Penlon Oxford ventilators Marks I and II: modification. SIB(87)84

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Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN. Pathogenic properties of invading micro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10: Data from the National Health Survey, No. 69*) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

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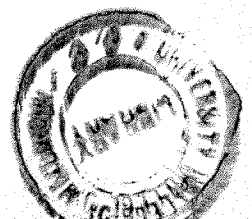
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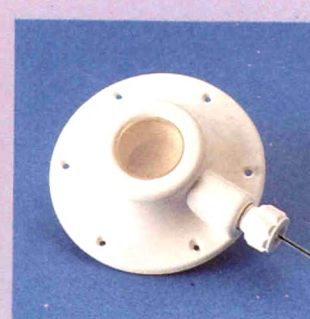
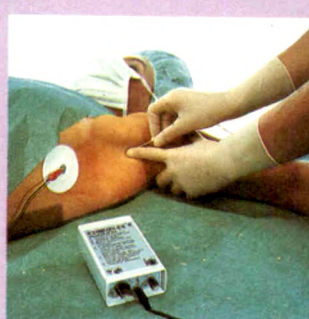
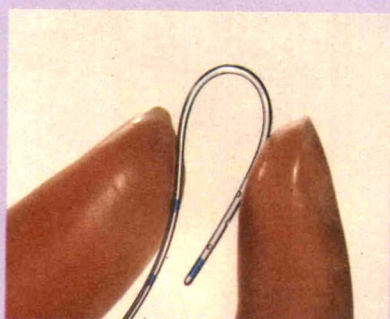
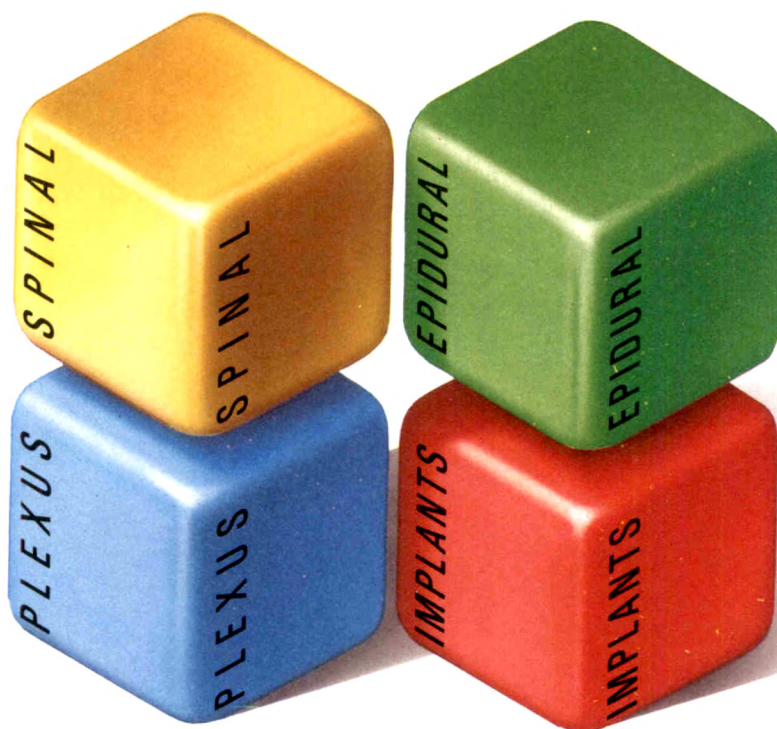
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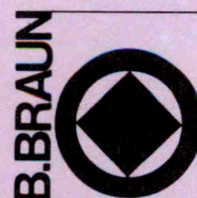
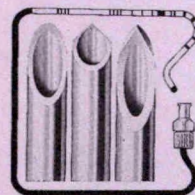
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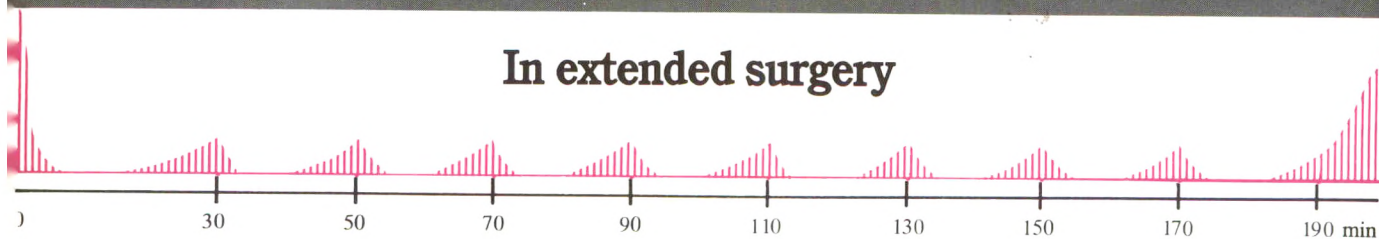
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2. Yate, P.M. *et al.* (1986), *Br. J. Anaesth.*, **58**, 112 S.

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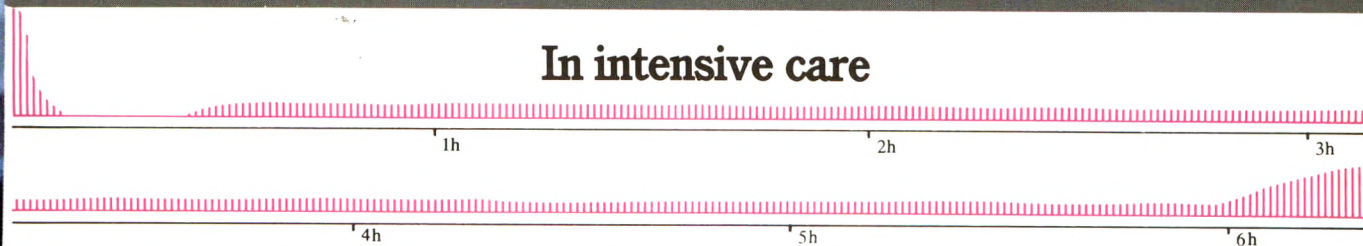


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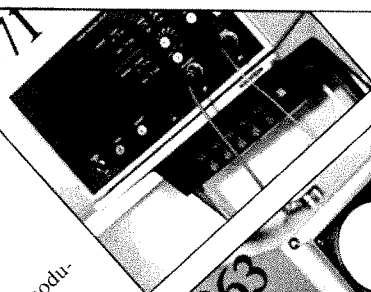
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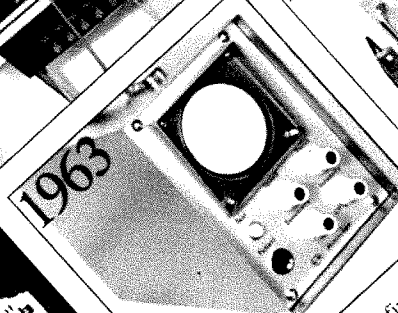
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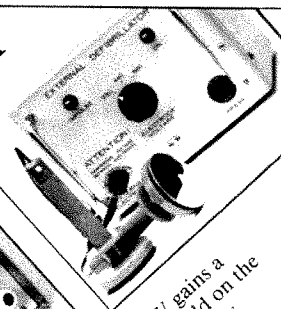
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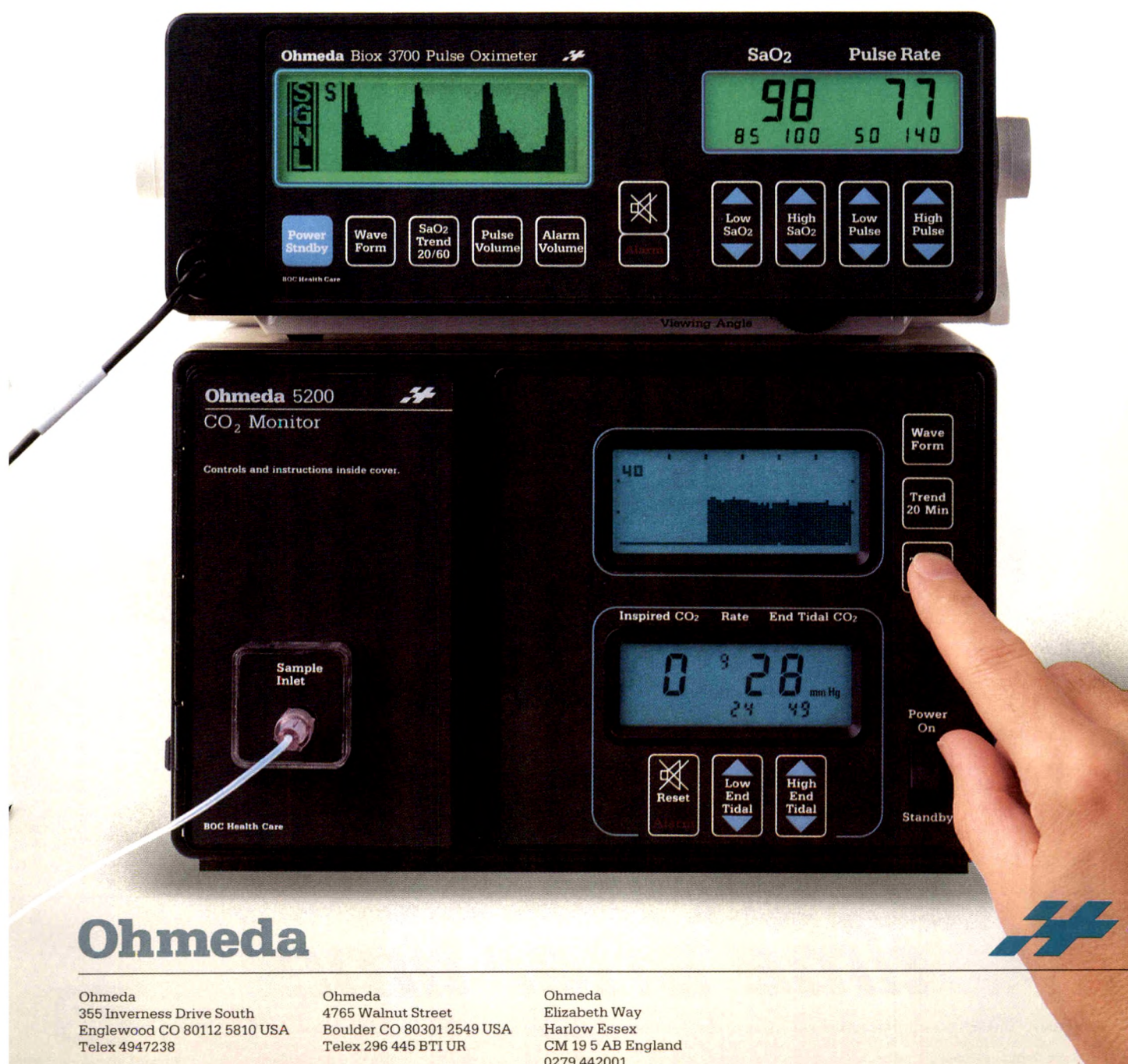
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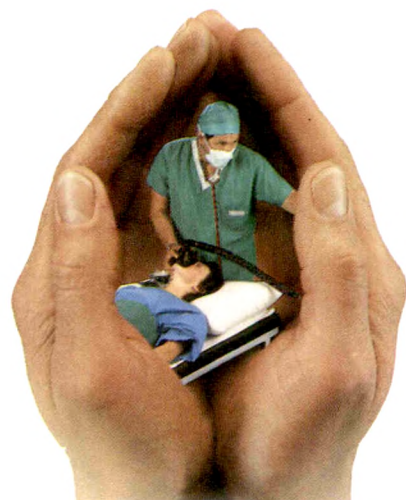
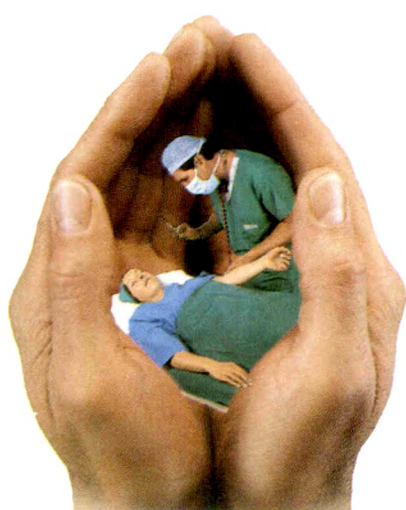
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Bladder temperature as an estimate of body temperature during cardiopulmonary bypass

M. E. BONE AND R. O. FENECK

Summary

Bladder temperature measured by a thermistor-tipped urinary catheter, was compared to oesophageal, nasopharyngeal, rectal and cutaneous temperatures in 33 patients during cardiopulmonary bypass. The bladder site was warmer than all other monitored sites in the pre-bypass period and showed least variation in temperature. The rate of change of bladder temperature during cooling and rewarming on bypass was significantly ($p < 0.01$) lower than for oesophageal and nasopharyngeal temperatures, but was greater than or similar to the rate of change of rectal and cutaneous temperatures. This method of temperature measurement was found to be satisfactory during major surgery and also during the postoperative period in the intensive care unit.

Key words

Monitoring; temperature.

Surgery; cardiac.

Body temperature monitoring is routine practice during cardiopulmonary bypass since patients may be actively cooled and rewarmed during the procedure. Various sites have been used to measure body temperature. These include nasopharyngeal,^{1,2} oesophageal^{1,3} cutaneous,⁴ rectal⁵ and tympanic⁶ temperatures. These sites serve two separate and distinct purposes: firstly, as an estimate of specific organ temperature, for example tympanic temperature as an estimate of brain temperature;⁶ and secondly, as a means of measuring whole body temperature, or core temperature. Many of these sites suffer from drawbacks for the latter purpose. In particular, temperature measurements in hollow viscera may simply record the temperature of the surrounding air or contents, and cutaneous temperatures are notoriously unreliable for the estimation of core temperature during cardiopulmonary bypass.

A new approach to this problem is the recent development of a urinary catheter with a thermistor tip. This catheter is connected to a device which measures bladder temperature and also urine flow. It has the advantage that it is sited in a fluid-filled viscus and gives accurate and reproducible temperature measurements.⁷ We compared temperatures measured from the bladder with those from oesophageal, nasopharyngeal, rectal and cutaneous sites in order to assess how bladder temperature varies from previously established methods of temperature measurement. Two groups of patients were investigated: those who

underwent cardiopulmonary bypass at 28°C, and those who underwent cardiopulmonary bypass without active whole body cooling but with simple drift of temperature to approximately 34°C.

Methods

Thirty-three patients scheduled to undergo cardiac surgery with cardiopulmonary bypass were studied. Informed consent for entry into the trial was obtained. Relevant anti-anginal medication was continued until induction of anaesthesia. Patients received a benzodiazepine and opiate premedication. Induction and maintenance of anaesthesia followed routine practice at the London Chest Hospital, with a combination of opiate, benzodiazepine and pancuronium with or without thiopentone. The patients' lungs were ventilated by intermittent positive pressure ventilation or by high frequency jet ventilation with a mixture of nitrous oxide and oxygen, or oxygen and air. All patients were perfused using a nonpulsatile pump and both bubble (Bently B10–10) and membrane (COBE) oxygenators were used. The bypass was primed with either crystalloid, or a mixture of crystalloid and blood, at room temperature.

A urinary bladder thermistor-tipped catheter (Vitalmetrics, Urine Monitoring System, Model 220) was placed after induction of anaesthesia. Bladder temperature was displayed on the digital readout of the monitor. Accessory

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Table 1. Patient demography.

	Group 1 (n = 15)	Group 2 (n = 18)
Mean (SEM) age, years	57.7 (1.7)	57.7 (1.7)
Sex, M:F	12:3	16:2
Mean (SEM) weight, kg	77.5 (3.1)	74.6 (2.8)
Mean (SEM) height, cm	172 (2.6)	170 (1.8)
Operation		
CAVG	9	18
Valve replacement	1	0
CAVG and valve replacement	3	0
CAVG and aneurysmectomy	2	0
Mean (SEM) anaesthetic time, minutes	189.0 (8.3)	184.2 (6.6)
Mean (SEM) surgical time, minutes	159.3 (8.6)	156.1 (8.0)
Mean (SEM) CPB time, minutes	71.8 (4.8)	79.9 (8.0)
Mean (SEM) aortic cross clamp time, minutes	40.7 (3.8)	35.8 (2.6)

CAVG, coronary artery vein graft; CPB, cardiopulmonary bypass.

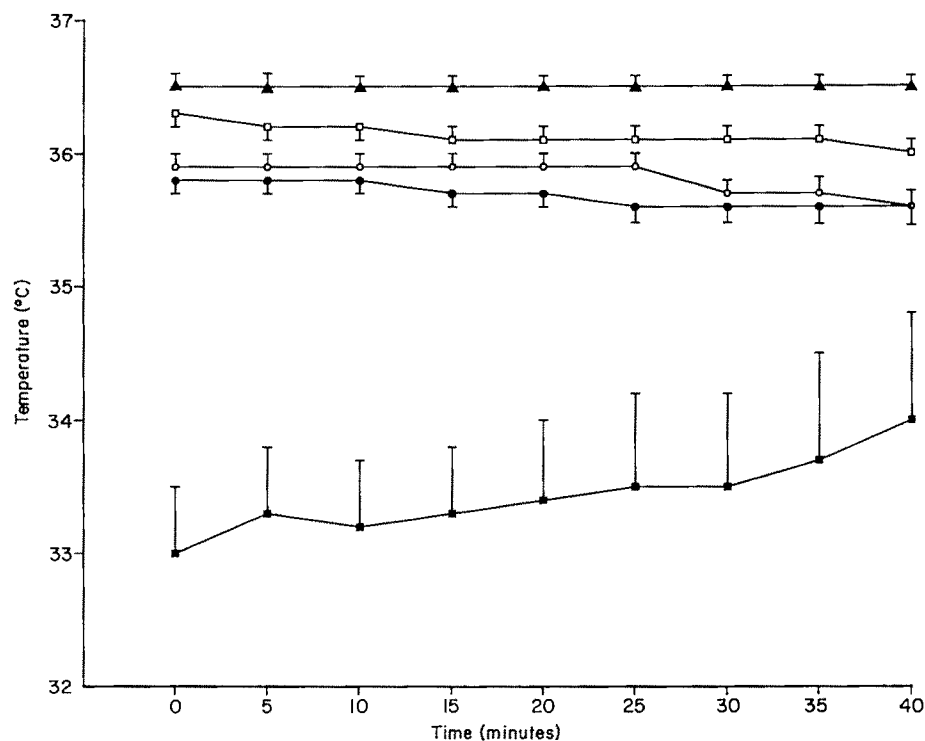


Fig. 1. Mean temperatures for all patients during the pre-bypass period, at oesophageal (●), nasopharyngeal (○), bladder (▲), rectal (□) and thumb (■) sites. Bars indicate SEM.

thermistor probes (Exacon) calibrated against a standard mercury-in-glass thermometer were placed as follows: in the nasopharynx, at the level of the posterior border of the soft palate; in the lower third of the oesophagus; in the rectum; and on the thumb contralateral to the radial arterial cannula. Temperature measurements from each site were recorded throughout the operation at intervals of 5 minutes.

The patients were assigned to one of two groups according to the method of cooling during cardiopulmonary bypass, which was selected according to the decision of the surgical team. Patients in group 1 were cooled to a target temperature of 28°C measured at the nasopharyngeal site; active cooling was not undertaken in group 2 but temperature was allowed to drift to approximately 34°C measured at the nasopharyngeal site. A Haemotherm heat exchanger was employed to cool and rewarm the patients during bypass, and the blood temper-

ature was recorded in the arterial outflow of the oxygenator. Myocardial preservation was achieved in group 1 with 20 mmol St Thomas' cardioplegia in 1000 ml Ringer's solution at 4°C. Theatre temperature was recorded at the start and end of surgery. Bladder temperature was monitored over a 12-hour period in five patients after transfer to the intensive care unit.

Statistical analysis of the temperatures was performed using two-way analysis of variance for each group of patients.

Results

Patient demographic data are presented in Table 1. The mean operating theatre temperature was 23°C (SEM 0.3).

Pre-bypass. Figure 1 shows the mean temperature at each site for all patients. Bladder temperature at the start of surgery was approximately 0.2°C greater than rectal temper-

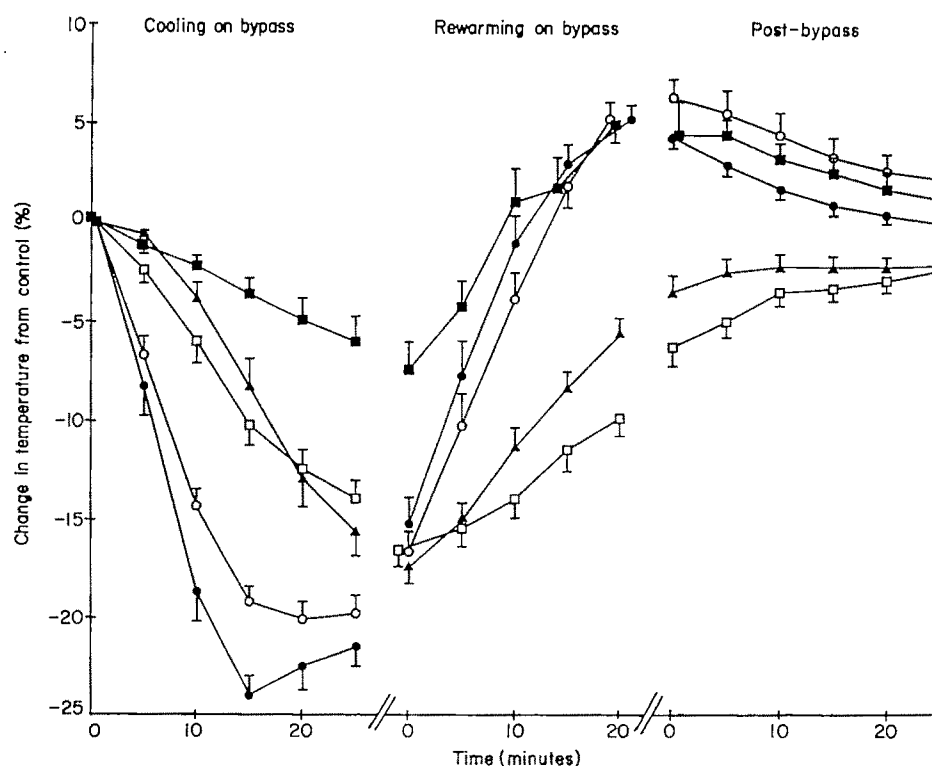


Fig. 2. Changes in temperature for group 1 shown as percentage change from control (at time of going onto bypass), during cooling on bypass, re-warming on bypass and post-bypass, at oesophageal (●), nasopharyngeal (○), bladder (▲), rectal (□) and thumb (■) sites. Bars indicate SEM.

Table 2. Mean (SEM) temperatures at time of going onto bypass.

Temperature, °C	Group 1	Group 2
Nasopharynx	35.0 (0.3)	35.6 (0.2)
Oesophageal	35.4 (0.2)	35.4 (0.2)
Bladder	36.3 (0.1)	36.4 (0.1)
Rectal	36.0 (0.1)	36.0 (0.1)
Thumb	34.5 (0.3)	33.3 (0.3)
Arterial inflow	26.4 (0.5)	32.8 (0.2)

ature, 0.6°C greater than nasopharyngeal temperature, 0.7°C greater than oesophageal temperature and 3.5°C greater than thumb temperature. The bladder showed least change in temperature during this period of unassisted circulation and significant differences ($p < 0.01$) were found between bladder temperature and those recorded at all other sites.

Group 1

Cooling on bypass. The percentage change in temperature from baseline (temperature at time of going onto bypass, Table 2) was calculated for each site (Fig. 2). The rate of decrease in temperature was greatest for the oesophageal site and least for the rectal site. During the period of cooling there were significant differences ($p < 0.01$) between bladder temperature compared with nasopharyngeal, oesophageal and thumb temperatures, but not rectal temperature. The greatest variations in temperature were recorded at 15 minutes, when oesophageal temperature showed a 24% change from baseline, bladder temperature an 8.5% change from baseline and thumb temperature was 4% below baseline. The temperature of the arterial inflow

blood increased slowly to 28.2°C during the cooling period.

Rewarming on bypass. The percentage change in temperature from baseline was similar at the start of rewarming for bladder, nasopharyngeal, oesophageal and rectal sites, namely between 15.5% and 17.5% below baseline values (Fig. 2). Actual temperatures at this time for these sites were 30.0°C, 29.1°C, 30.0°C and 30.0°C, respectively. The temperature of the arterial inflow blood increased from 28.9°C to a maximum of 38.0°C at 20 minutes after the start of rewarming. The greatest rates of temperature increase occurred at the oesophageal and nasopharyngeal sites. The bladder and rectal temperatures increased more slowly. Oesophageal, nasopharyngeal and thumb sites demonstrated an increase of 5% from their baseline values at 20 minutes after initiation of rewarming, while the bladder and rectal temperatures remained below their control values. There were significant differences ($p < 0.01$) in temperature of the bladder site compared to all other sites during the period of rewarming.

Post-bypass. All temperatures tended to return to their baseline values. The oesophageal temperature returned to its original value at 25 minutes. Nasopharyngeal and thumb temperatures remained above, and bladder and rectal temperatures remained below their baseline values. Significant differences ($p < 0.01$) were found between bladder temperature and temperature at all other sites during this period of unassisted circulation.

Group 2

The overall changes in temperature in this group were less than in the actively cooled group.

Drifting of temperature on bypass. The percentage change

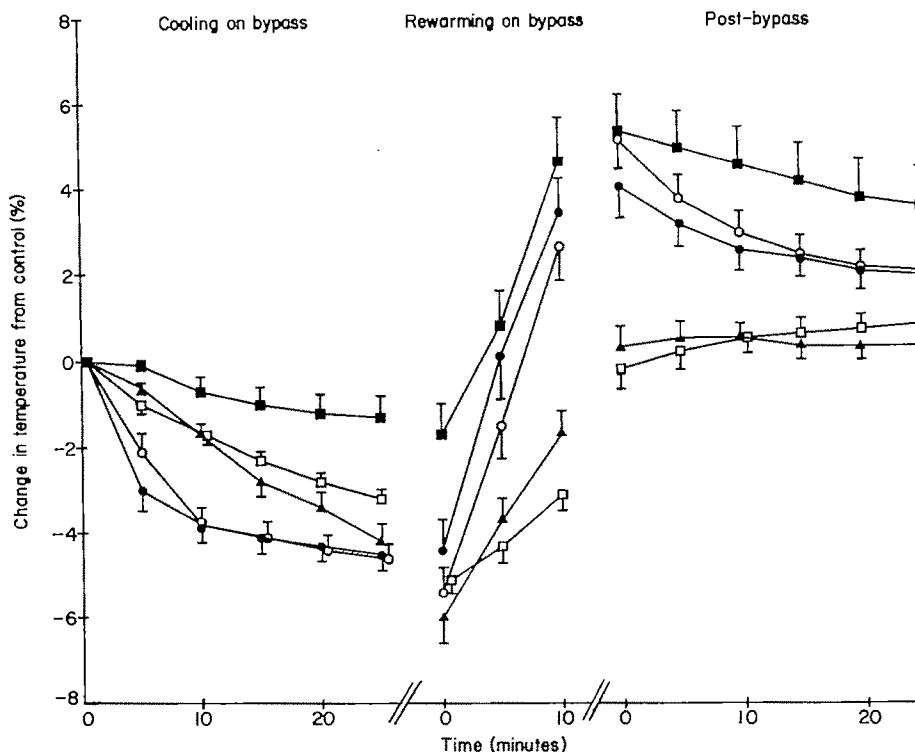


Fig. 3. Changes in temperature for group 2 shown as percentage change from control (at time of going onto bypass), during cooling on bypass, re-warming on bypass and post-bypass, at oesophageal (●), nasopharyngeal (○), bladder (▲), rectal (□) and thumb (■) sites. Bars indicate SEM.

in temperature from baseline (temperature at time of going onto bypass, Table 2) was calculated for each site. Oesophageal and nasopharyngeal sites demonstrated the greatest percentage changes in temperature (Fig. 3). There were significant differences ($p < 0.01$) between bladder temperature and all sites except the rectum.

Rewarming on bypass. Bladder temperature showed the greatest percentage change from baseline at the start of rewarming. The temperature of the arterial inflow blood increased from 33.3°C to 38.2°C at 15 minutes, and the nasopharyngeal, oesophageal and thumb sites showed increases above their baseline temperature at 10 minutes after the start of rewarming. There were significant differences ($p < 0.01$) in the change in bladder temperature compared with all sites except the rectum during this period.

Post-bypass. All values, except rectal, were above baseline at the time of coming off bypass; oesophageal, nasopharyngeal and thumb values were greatest. All temperatures then returned to their baseline values. Significant differences ($p < 0.01$) were found, as before, in this group of patients.

The use of the thermistor-tipped urinary catheter was found to be satisfactory in all patients studied and there were no adverse effects. The catheters remained *in situ* while the patients were nursed in the intensive care unit. Urinary bladder temperature monitoring was undertaken post-operatively in five of the patients and was acceptable to patients and to nursing staff.

Discussion

Accurate estimates of core body temperature are important in patients who undergo open heart surgery. The safe duration of circulatory arrest is limited by the viability of

the central nervous system and is dependent on the temperature of the brain at the moment that blood flow is stopped.⁴ A major risk during the transition phases of cooling and rewarming, is the development of large thermal gradients in the body tissues, which imply slow heat transfer and an increased risk of imbalance between metabolite supply and demand. Rewarming should continue until a reasonable core temperature is achieved. The nasopharyngeal and oesophageal temperatures are measured in areas of high blood flow and represent measurements of temperature of blood received from the extracorporeal system. The rectal temperature is measured in a low blood flow area but shows an excessively long lag period. Bladder temperature may offer a more acceptable measurement for areas of intermediate blood flow.

Various sites have been employed to estimate body temperature but each has advantages and drawbacks. Davis² found that nasopharyngeal temperature reflected core temperature accurately in the steady state. Others^{8,9} have considered it to be an unreliable estimate of core temperature. Lower oesophageal temperature readings give an approximate estimate of cerebral temperature but are unreliable with an open thorax and during rapid transfusion of cold blood.¹ Middle and lower oesophageal temperatures are affected by ventilation.³ Tympanic and oesophageal temperature measurements have been found to be mutually consistent during anaesthesia.⁶ Changes in rectal temperature were found to lag behind oesophageal temperature in patients who were cooled during cardiopulmonary bypass.⁵ The rectal site also has the disadvantage of a large drift in temperature after rewarming. The intravascular site has been shown to demonstrate the most rapid temperature changes² but is invasive and not widely employed.

Clearly, no ideal site exists for estimates of core body temperature. MacDonald¹⁰ found in a survey of centres of cardiac surgery in the United Kingdom, that temperature monitoring was performed most commonly at two sites, namely, oesophagus and nasopharynx, or oesophagus and rectum. Bladder temperature may offer an alternative site for the second measurement and represents an area of intermediate blood flow.

The present study was undertaken to compare a recently introduced method of monitoring body temperature with previously established techniques. We found that at steady state, the bladder temperature was slightly higher than at any other site. This is not unexpected, since urine, a filtrate of blood, may accurately reflect blood temperature. All other sites demonstrated variable drift in temperature during this period.

The greatest changes in temperature during the periods of active cooling and rewarming occurred at sites most exposed to the inflow from the pump, i.e. the oesophageal and, later, the nasopharyngeal sites. Changes in temperature at the rectal site lagged behind all others. This could be due to this area's low blood flow and also to the presence of rectal contents that form a thermal reservoir. The temperature changes at the bladder site during periods of cooling and rewarming fell between oesophageal and nasopharyngeal, and rectal. This site could therefore be employed in place of the rectal site. Indeed, oesophageal, nasopharyngeal, bladder and rectal temperatures showed similar changes from baseline at the start of rewarming in both groups, and the actual readings were within 1°C of each other. The oesophageal and nasopharyngeal sites, however, showed an 'overswing' before they returned to this temperature. Bladder temperature returned to within 2% of its baseline value 25 minutes after completion of bypass. A previous study⁷ showed a good correlation between urinary bladder, oesophageal, rectal and pulmonary artery temperatures during bypass but the rate of change in temperature at the bladder site was greater than at the oesophageal site. This is in contrast to our findings.

Long-term monitoring of temperature in the intensive care unit is fraught with problems. Rectal probes are prone to be extruded and oesophageal temperature monitoring is not widely practised. Bladder temperature was monitored

postoperatively in five patients in this study and found to be highly acceptable. This method of temperature monitoring may also be of particular value during long surgical procedures such as vascular surgery, when both temperature and urinary outflow are measured. We found no problems during catheterisation of patients.

In conclusion, bladder temperature appears to offer a convenient estimate of core body temperature in patients who undergo cardiac surgery. The rate of change in temperature at this site lags behind those sites more directly exposed to the temperature swings during active cooling and rewarming on bypass but responds more rapidly than the rectal site. This clean, noninvasive method of measuring temperature was found to be safe, convenient and accurate both during surgery and in the intensive care unit.

References

1. WHITBY JD, DUNKIN LJ. Cerebral, oesophageal and nasopharyngeal temperatures. *British Journal of Anaesthesia* 1971; **43**: 673-6.
2. DAVIS FM, PARIMELAZHAGEN KN, HARRIS EL. Thermal balance during cardiopulmonary bypass with moderate hypothermia in man. *British Journal of Anaesthesia* 1977; **49**: 1127-32.
3. WHITBY JD, DUNKIN LJ. Temperature differences in the oesophagus. The effects of intubation and ventilation. *British Journal of Anaesthesia* 1969; **41**: 615-8.
4. HERCUS V, COHEN D, BOWRING AC. Temperature gradients during hypothermia. *British Medical Journal* 1959; **1**: 1439-41.
5. COOPER KE, KENYON JR. A comparison of temperatures measured in the rectum, oesophagus and on the surface of the aorta during hypothermia in man. *British Journal of Surgery* 1957; **44**: 616-9.
6. BENZINGER M. Tympanic thermometry in surgery and anaesthesia. *Journal of the American Medical Association* 1969; **209**: 1207-11.
7. LILLY JK, BOLAND JP, ZEKAM S. Urinary bladder temperature monitoring: a new index of core body temperature. *Critical Care Medicine* 1980; **8**: 742-4.
8. STUPFEL M, SEVERINGHAUS JW. Internal body temperature gradients during anesthesia and hypothermia and effect of vagotomy. *Journal of Applied Physiology* 1956; **9**: 380-6.
9. COHEN D, HERCUS V. Controlled hypothermia in infants and children. *British Medical Journal* 1959; **1**: 1435-9.
10. MACDONALD DJF. Current practice of hypothermia in British cardiac surgery. *British Journal of Anaesthesia* 1975; **47**: 1011-7.

Prolonged anaesthesia with isoflurane and halothane

Effects on hepatic function

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A. M. KLEIN AND W. F. DICK

Summary

Hepatic function was assessed pre-operatively and on the first and sixth postoperative days in 40 healthy patients who underwent prolonged maxillofacial surgery with isoflurane or halothane anaesthesia. No major changes were observed in hepatic enzymes or bilirubin. One-stage prothrombin time and Factor VII concentrations decreased on the first postoperative day and this change was more pronounced in the halothane group. The results support the use of isoflurane rather than halothane for prolonged anaesthesia in respect of the synthesising function of the liver.

Key words

Anaesthetics, volatile; isoflurane, halothane.

Complications; hepatic.

The mechanism of hepatic damage produced by volatile anaesthetics remains unknown, although the subject has been studied extensively.¹ There is some evidence that halothane is potentially hepatotoxic² but the cause of hepatic impairment after enflurane and isoflurane anaesthesia remains unresolved.^{3,4} A differential pathogenesis was recently suggested which indicated a chemotoxic mechanism for halothane and a predominantly hypoxic mechanism for enflurane.⁵ Duration of anaesthesia contributes to toxicity.⁶ It has been claimed, based on a pharmacological rationale, that isoflurane is the volatile agent of choice for prolonged anaesthesia^{7–9} although clinical studies on the subject are scarce. We investigated the effects of prolonged isoflurane and halothane anaesthesia on biochemical and haematological measurements of hepatic function. Other factors known to contribute to liver damage were avoided.

Methods

Forty adult patients of ASA grades 1 or 2 who presented for maxillofacial surgery were assigned randomly to receive either isoflurane ($n = 20$) or halothane ($n = 20$). Institutional approval and informed consent to participate in the study were obtained. Subjects who presented with clinical evidence or history of hepatic or gastrointestinal disease, coagulopathy, hypertension, alcoholism, drug abuse, dia-

betes or alimentary disorders were excluded from the study. Prolonged anaesthesia was defined as ≥ 180 minutes of isoflurane/halothane administration. Premedication consisted of an oral benzodiazepine (flunitrazepam 1–2 mg) at night and on the morning of surgery. Induction of anaesthesia followed a 10-minute period of pre-oxygenation and was achieved by intravenous administration of fentanyl 5 $\mu\text{g}/\text{kg}$ and etomidate 0.2 mg/kg. Neuromuscular blockade was achieved with vecuronium 0.1 mg/kg. Intravenous fluid administration was limited to crystalloids. No blood or blood products were given.

After tracheal intubation, anaesthesia was maintained by controlled ventilation with isoflurane 0.6% or halothane 0.35% (end tidal concentrations) in nitrous oxide and oxygen (FiO_2 0.35); these concentrations of isoflurane and halothane, in combination with nitrous oxide 65%, were calculated to achieve a total of 1.3 MAC (minimum alveolar concentration) of inhalational anaesthetic in each group. A minimal flow technique with fresh gas flows between 400 and 500 ml/minute was used. Ventilation was adjusted to achieve an end tidal carbon dioxide concentration of 4.6–5.3%. Repeat doses of fentanyl and vecuronium were given as required. Monitoring included electrocardiogram, arterial blood pressure, temperature, relaxometry, inspired and expired oxygen concentrations, end tidal carbon dioxide concentration, isoflurane/halothane concentration (Normac, Datex) and nitrous oxide concentration (Irina,

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Draeger). Oxygen saturation during recovery was monitored by pulse oximetry (Nellcor). Blood samples were taken on three mornings; pre-operatively (baseline) and on the first and sixth postoperative days. The samples were analysed for parameters of structural integrity (aspartate aminotransferase (AST), alanine aminotransferase (ALT), glutamate dehydrogenase (GLDH), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (G-GT)) and functional integrity (detoxifying function (bilirubin), synthesising function (one-stage prothrombin time, Factor V, Factor VII)). The one-stage prothrombin time (Quick's time) was measured with a single charge of thromboplastin/ Ca^{2+} in all patients. For each time value, the corresponding clotting activity value (PT) was derived from a standard nomogram and expressed as a percentage of the institutional normal value (physiological range: PT $\geq 70\%$). The same procedure was used to express Factor V and Factor VII. A low percentage value for any of these variables indicates reduced clotting activity.

Statistical significance was assessed using the Wilcoxon signed rank test and assumed at $p \leq 0.01$.

Results

Exposure time was 291 (S.D. 68) minutes (range 180–390) for isoflurane and 298 (S.D. 76) minutes (range, 180–495) for halothane. Circulatory and respiratory variables remained within normal ranges throughout the study in all patients.

Laboratory data for the pre-operative values and those on the first and sixth postoperative days are presented in Figs 1–3. In neither group were there changes in AST or GLDH. ALT and G-GT were increased on the sixth postoperative day, and this change was more pronounced in the halothane group. A decrease occurred on day 1 for AP in the isoflurane group and on day 6 for bilirubin in both groups. Factor V remained unchanged but Factor VII and PT decreased significantly on the first postoperative day with a subsequent recovery to baseline by day 6. The decreases in PT and Factor VII on day 1 were more pronounced in patients who received halothane, and included values far below the physiological range.

Discussion

The mechanisms that underlie anaesthesia-induced hepatic injury are unknown. Prolonged anaesthesia is considered to be a risk factor.⁶ Data on hepatic function after prolonged inhalational anaesthesia in man are rare. Other risk factors were eliminated in this study by selecting fit patients¹⁰ undergoing peripheral surgery,¹¹ by avoiding drugs which are hepatotoxic or known to induce enzyme induction and by extensive monitoring to ensure the absence of hypoxaemia, hypo- or hypercapnia, and hypo- or hyperthermia.

Measurement of serum concentrations of liver enzymes is the most common method of testing for hepatic injury after general anaesthesia.^{6,12–14} A combined analysis of ALT, AST, G-GT, AP and bilirubin allows detection of hepatobiliary disease with a sensitivity of $\geq 95\%$.¹⁵ However, the relevance of elevated levels of AP and G-GT to the diagnosis of anaesthetic-induced hepatic injury is controversial.^{14,16–18} The value of some clotting tests for assessment of hepatic function was recently emphasised.^{19,20}

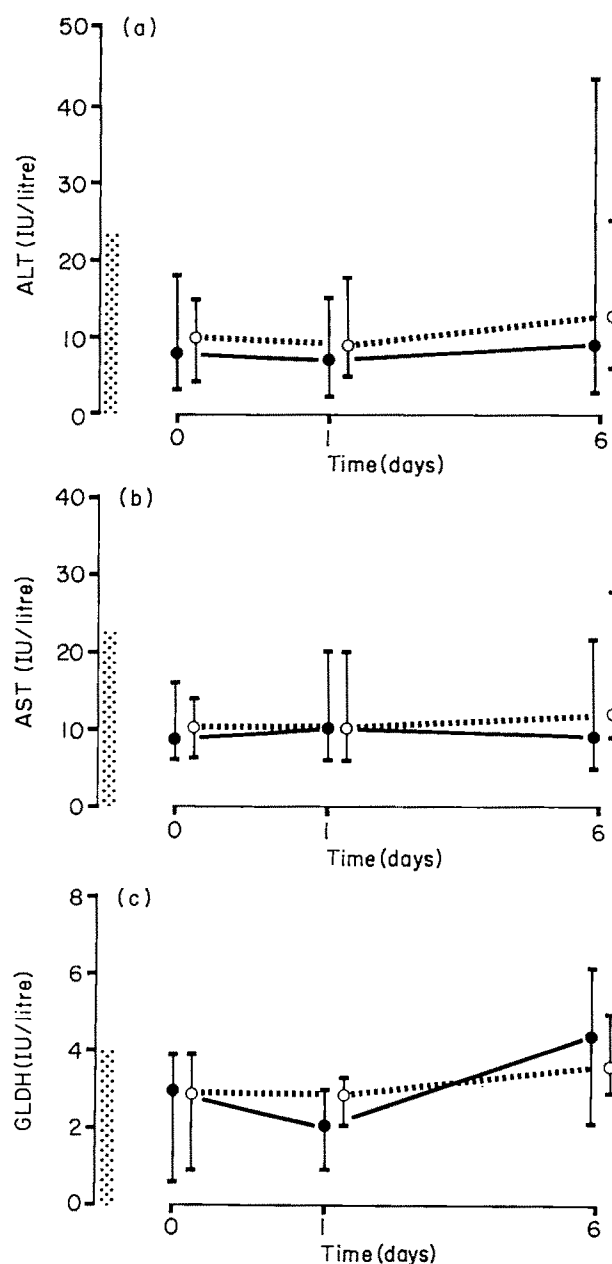


Fig. 1. (a) ALT changes, (b) AST changes and (c) GLDH changes following prolonged anaesthesia with isoflurane (●) and halothane (○) (median, range). Dotted column indicates physiological range.

No significant changes from baseline values were found for the transaminases in the present study. However, there were small changes in a number of patients and these included both increases and decreases. Similar observations were made previously after halothane anaesthesia¹² and no significant changes were found in a study of 51 patients subjected to prolonged surgery with isoflurane-nitrous oxide anaesthesia.²¹ Zinn *et al.*²² found a decrease in ALT and AST after enflurane anaesthesia in patients with mild alcoholic hepatitis.

A slight decrease in AP was found on the first postoperative day and for bilirubin on the sixth day in both groups in the present study. G-GT increased to above control on the sixth day. These findings are in accordance with previous reports.⁶ It appears that liver enzyme determinations are insufficiently sensitive to detect reliably, inconsequential hepatic dysfunction. There were significant decreases in

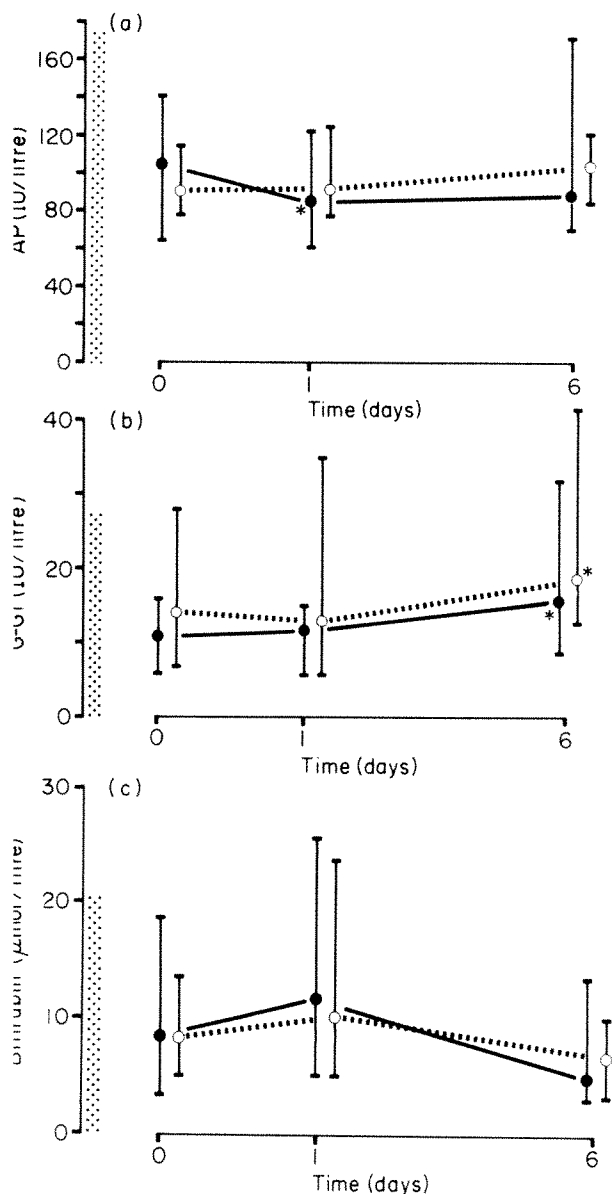


Fig. 2. (a) AP changes, (b) G-GT changes and (c) bilirubin changes following prolonged anaesthesia with isoflurane (●) and halothane (○) (median, range). Dotted column indicates physiological range; asterisk indicates significant change from baseline ($p \leq 0.01$).

Factor VII and PT on the first postoperative day, with subsequent recovery to baseline values on the sixth day. This observation is in agreement with reports on enflurane.²³ The decrease was more pronounced in the halothane group, and included values which were below the physiological minimum and thus of possible clinical relevance. Factor V (plasma half-life 12–15 hours) remained unchanged throughout the study in both groups and so haemodilution can be excluded as a cause for the observed decrease in Factor VII (plasma half-life 2–5 hours) concentration.

We suggest that the decrease in Factor VII and PT on the first postoperative day reflects a reduced synthesising activity of the liver, which indicates subclinical hepatic compromise. Reduction in hepatic blood flow is a possible cause. Whether such a decrease of perfusion is due to positive pressure ventilation, to the volatile agent or to other causes remains to be clarified. However, since anaesthetic

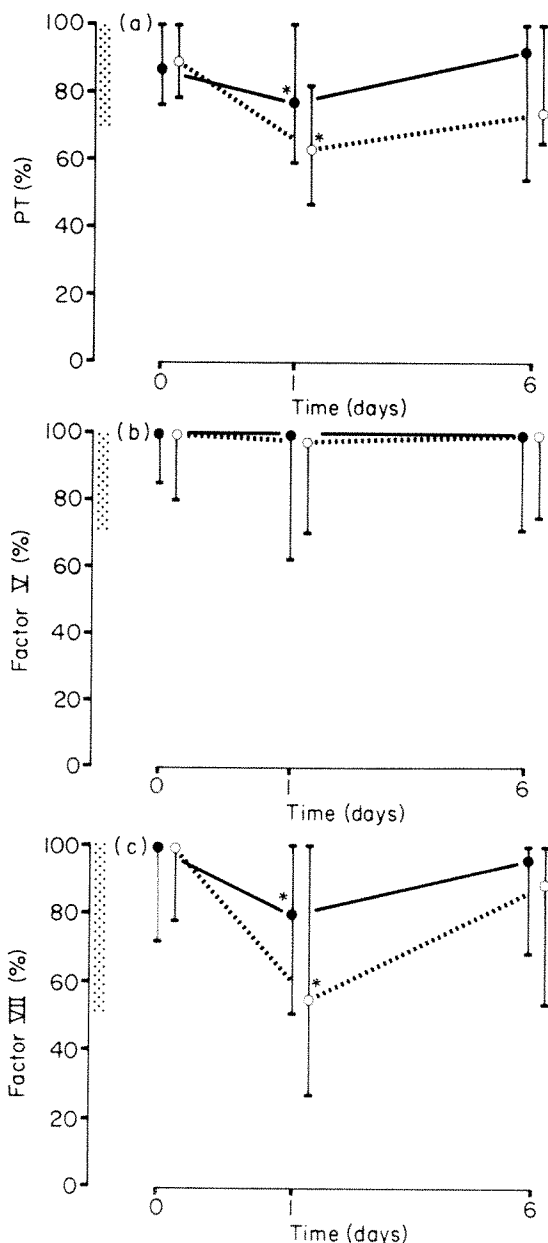


Fig. 3. (a) Changes in one-stage prothrombin time (PT), expressed as percentage of normal clotting, (b) Factor V changes (percentage of normal) and (c) Factor VII changes (percentage of normal) following prolonged anaesthesia with isoflurane (●) and halothane (○) (median, range). Dotted column indicates physiological range; asterisk indicates significant change from baseline ($p \leq 0.01$).

and surgical management was otherwise similar in both groups, the observed differences in PT and Factor VII activities may be ascribed to the volatile agent. Volatile anaesthetics have been shown to reduce hepatic blood flow, possibly by mechanisms mediated through the sympathetic nervous system.^{24,25} Blood flow through the portal vein is reduced by halothane and isoflurane but there is a compensatory increase in hepatic artery perfusion with isoflurane.²⁶ This may account for the less pronounced changes observed in the isoflurane group in the present study. However, changes were also seen with isoflurane, which suggests that total hepatic blood flow may not be maintained with either anaesthetic. This finding is supported by recent animal studies.^{27,28}

In conclusion, we found that hepatic function was altered after prolonged anaesthesia with either isoflurane or halothane. Factor VII activity was depressed to a greater degree in the halothane group. Our results support the use of isoflurane rather than halothane for prolonged anaesthesia.

Acknowledgment

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References

- BROWN BR, GANDOLFI AJ. Adverse effects of volatile anaesthetics. *British Journal of Anaesthesia* 1987; **59**: 14-23.
- BLOGG CE. Halothane and the liver: the problem revisited and made obsolete. *British Medical Journal* 1986; **292**: 1691-2.
- EGER EI, SMUCKLER EA, FERRELL LD, GOLDSMITH CH, JOHNSON BH. Is enflurane hepatotoxic? *Anesthesia and Analgesia* 1986; **65**: 21-30.
- STOELTING RK, BLITT CD, COHEN PJ, MERIN RG. Hepatic dysfunction after isoflurane anesthesia. *Anesthesia and Analgesia* 1987; **66**: 147-53.
- LIND RC, GANDOLFI AJ, SIPES G, BROWN BR. Comparison of the requirements for hepatic injury with halothane and enflurane in rats. *Anesthesia and Analgesia* 1985; **64**: 955-63.
- STEVENS WC, EGER EI, JOAS TA, CROMWELL TH, WHITE A, DOLAN WM. Comparative toxicity of isoflurane, halothane, fluoroene and diethyl ether in human volunteers. *Canadian Anaesthetists' Society Journal* 1973; **20**: 357-68.
- KOFKE WA, SNIDER MT, YOUNG RSK, RAMER JC. Prolonged low flow isoflurane anesthesia for status epilepticus. *Anesthesiology* 1985; **62**: 653-6.
- PEARSON J. Prolonged anesthesia with isoflurane. *Anesthesia and Analgesia* 1985; **64**: 92-3.
- WAGENER B, HEMPEL V, STÜTZLE V. Isofluran zur Langzeit-sedierung bei Respirator-Behandlung. Fluoridspiegel in Serum und Urin (Abstract). *Anaesthesist* 1986; **35**: 124.
- SCHEMEL WH. Unexpected hepatic dysfunction found by multiple laboratory screening. *Anesthesia and Analgesia* 1976; **55**: 810-2.
- CLARKE RSJ, DOGGART JR, LAVERY T. Changes in liver function after different types of surgery. *British Journal of Anaesthesia* 1976; **48**: 119-28.
- AKDIKMEN SA, FLANAGAN TV, LANDMESSER CM. A comparative study of serum glutamic pyruvic transaminase changes following anesthesia with halothane, methoxyflurane, and other inhalation agents. *Anesthesia and Analgesia* 1966; **45**: 819-25.
- DUNDEE JW, MCILROY PDA, FEE JPH, BLACK GW. Prospective study of liver function following repeat halothane and enflurane. *Journal of the Royal Society of Medicine* 1981; **74**: 286-91.
- FEE JPH, BLACK GW, DUNDEE JW, MCILROY PDA, JOHNSTON HML, JOHNSTON SB, BLACK IHC, McNEILL HG, NEILL DW, DOGGART JR, MERRETT JD, McDONALD JR, BRADLEY DSG, HAIRE M, McMILLAN SA. A prospective study of liver enzyme and other changes following repeat administration of halothane and enflurane. *British Journal of Anaesthesia* 1979; **51**: 1133-40.
- FERRARIS R, COLOMBATTI G, FIORENTINI MT, CAROSSO R, AROSSA W, DE LA PIERRE W. Diagnostic value of serum bile acids and routine liver function tests in hepatobiliary diseases. Sensitivity, specificity, and predictive value. *Digestive Diseases and Sciences* 1983; **28**: 129-36.
- McLAUGHLIN DF, EGER EI. Repeated isoflurane anesthesia in a patient with hepatic dysfunction. *Anesthesia and Analgesia* 1984; **63**: 775-8.
- LAMBERT DH. Isoflurane and hepatic function. *Anesthesia and Analgesia* 1985; **64**: 458-9.
- McLAUGHLIN DF, EGER EI. Isoflurane and hepatic function. *Anesthesia and Analgesia* 1985; **64**: 459-60.
- THALER H, LECHNER K. Einsatz von Blutgerinnungstesten bei der Diagnostik und Überwachung von Patienten mit Lebererkrankungen. (The use of blood coagulation test in the diagnosis and monitoring of patients with liver diseases.) *Hämostaseologie* 1984; **2**: 39-42.
- CORRIGAN JJ JR. Diagnosis and therapy of coagulopathies in patients with liver disease. In: BROWN BR, ed. *Anesthesia and the patient with liver disease. Contemporary anesthesia practice*. Philadelphia: F.A. Davis Co., 1981: 1-11.
- MANNI C, PELOSI G, CAMAJONI D, PIETRINI D, RODOLA F, BURZA M. Isoflurane in prolonged and repeated anaesthesia. In: LAWIN P, VAN AKEN H, PUCHSTEIN C, eds. *Isoflurane. Anaesthesiology and intensive care medicine, Vol. 182*. Berlin: Springer-Verlag, 1986: 52-5.
- ZINN SE, FAIRLEY HB, GLENN ID. Liver function in patients with mild alcoholic hepatitis, after enflurane, nitrous oxide-narcotic, and spinal anesthesia. *Anesthesia and Analgesia* 1985; **64**: 487-90.
- POPOV-CENIC S, MÜLLER N, KLADETZKY RG, HACK G, LANG U, SAFER A, RAHLFS VW. Effects of premedication, narcosis and surgery on the coagulation and fibrinolysis systems and the platelets. The influence of dextran and hydroxy ethyl starch (HES) during and after operation. *Anaesthesist* 1977; **26**: 77-84.
- GELMAN S, FOWLER KC, SMITH LR. Regional blood flow during isoflurane and halothane anesthesia. *Anesthesia and Analgesia* 1984; **63**: 557-65.
- TVERSKOY M, GELMAN S, FOWLER KC, BRADLEY EL. Intestinal circulation during inhalation anesthesia. *Anesthesiology* 1985; **62**: 462-9.
- GELMAN S, FOWLER KC, SMITH LR. Liver circulation and function during isoflurane and halothane anesthesia. *Anesthesiology* 1984; **61**: 726-30.
- HOBBAHN J, CONZEN P, GOETZ A, HABAZETTL H, BRENDL W, PETER K. Liver perfusion and oxygenation with isoflurane. *Anästhesie, Intensivtherapie, Notfallmedizin* 1986; **21**: 85-9.
- KOSAKA F, YAMADA T, TANIGUCHI M, HIRAI Y, NISHIZAKI S, SAKANO N, KOSAKA M, KONDOU T. Alterations in hepatic blood flow during halothane, enflurane and isoflurane inhalation in dogs. *Anesthesiology* 1986; **65**: A566.

Patient-controlled analgesia with a mixture of pethidine and doxapram hydrochloride

A comparison of the incidence of respiratory dysrhythmias with pethidine alone

P. A. CLYBURN AND M. ROSEN

Summary

Twenty-four patients who underwent elective cholecystectomy received double-blind increments of either pethidine 30 mg or a mixture of pethidine 30 mg and doxapram 45 mg delivered on a patient-controlled basis. A loading dose of doxapram 100 mg or saline was administered. There was no difference in respiratory depression as indicated by respiratory frequency and end tidal carbon dioxide concentration. The incidence of respiratory apnoea was similar in the two groups but apnoea was of shorter duration in patients who received doxapram, although the difference was not significant. Patients who received doxapram assessed overall pain as worse on a linear analogue scale ($p < 0.05$) but demanded similar amounts of pethidine. There was no difference in pain on movement.

Key words

Analgesics, narcotic; pethidine.

Pain; postoperative.

Opioid analgesics cause progressive central respiratory depression. Intravenous opioid infusions after upper abdominal surgery have been reported to be associated with a high incidence of apnoeic episodes.^{1,2} There is an increase in both central and obstructive apnoea, the latter particularly associated with marked arterial oxygen desaturation.^{3,4} Patient-controlled analgesia (PCA) tailors the opioid administration to the patient's individual requirements and thus should be safer. However, there must still remain concern over the potential danger of respiratory dysrhythmias.

Doxapram hydrochloride is a respiratory stimulant with both central⁵ and peripheral action.⁶ Intravenous administration of doxapram in the postoperative period decreases depression of tidal volume, minute volume and arterial oxygen partial pressure.⁷ It causes a decrease in postoperative chest complications when infused intermittently,^{8–10} despite its short half-life. The present study compared the effect of concurrent administration of doxapram with pethidine and pethidine alone, both delivered by PCA in the postoperative period, on the incidence of respiratory dysrhythmias.

Methods

Twenty-four patients scheduled to undergo elective cholecystectomy gave informed consent to participate in the study, which was approved by the District Ethical Com-

mittee. Patients were instructed in the use of the Cardiff Palliator during the pre-operative visit, and randomly allocated to receive either pethidine or a mixture of pethidine with doxapram on each demand for postoperative analgesia. The two drug preparations were made up identically to provide double-blind conditions.

Patients were premedicated with oral diazepam 10 mg one hour pre-operatively. Anaesthesia was induced with thiopentone 3–4 mg/kg, tracheal intubation facilitated with suxamethonium or a non-depolarising muscle relaxant, and the patients' lungs ventilated with nitrous oxide and oxygen supplemented by a volatile agent. Up to 200 µg fentanyl was used for intra-operative analgesia. Residual muscle relaxation at the end of surgery was antagonised by neostigmine and atropine and the trachea extubated on resumption of spontaneous respiration.

A Cardiff Palliator was connected to the patient's intravenous infusion using a valved Y-connector¹¹ on arrival in the recovery ward. A slow intravenous loading dose of doxapram 100 mg in 5 ml was given to patients in the doxapram group and normal saline 5 ml, as an identical preparation, to those in the control group. Any adverse reaction to this administration was noted. The Palliator was set to administer increments of pethidine 30 mg with or without doxapram 45 mg, with a minimum interval of 10 minutes between doses. Patients were kept in the recovery room until they were able to use the Palliator without assistance. Intramuscular metoclopramide 10 mg was

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Table 1. Patient data.

	Number of patients	Mean (range) age, years	Sex ratio, F:M	Mean (range) weight, kg
Pethidine alone	11	45.7 (29-65)	10:1	71.0 (45-104)
Pethidine + doxapram	13	44.7 (21-63)	8:5	70.1 (55-100)

Table 2. Number of Palliator demands and antiemetic requirements.

	Mean (range) number of Palliator demands	Number of patients who required antiemetics	Mean (range) doxapram consumption, mg
Pethidine alone	13.5 (7-21)	7	—
Pethidine + doxapram	14 (4-25)	9	100 + 630 (180-1125)

Table 3. Mean (range) linear analogue scores in pethidine and pethidine + doxapram groups.

	Pethidine alone	Pethidine + doxapram	Significance
Drowsiness	48.6 (9-16)	65.5 (37-78)	$p < 0.1$
Nausea	27.2 (3-60)	30.1 (0-73)	NS
Happiness	28.9 (0-92)	37.3 (0-92)	NS
Depression	13.4 (0-47)	13.1 (0-61)	NS
Dizziness	25.4 (0-69)	25.8 (0-90)	NS
Amnesia	43.4 (0-92)	64.2 (23-100)	$p < 0.1$
Pain overall	38.4 (16-72)	58.7 (14-89)	$p < 0.05$
Pain at rest	26.9 (0-74)	6.4 (0-78)	$p < 0.1$
Pain on movement	67.5 (15-100)	66.8 (15-90)	NS

NS, $p > 0.1$.

prescribed for any patient who complained of nausea or who vomited.

Respiration was monitored continuously using a calibrated infrared carbon dioxide analyser (Datex) with sampling at the nares by means of a pair of fine catheters (2 mm external diameter). Airflow at the nose was detected as swings in carbon dioxide concentration upon inspiration and expiration. The analogue output from this monitor was recorded on a two-channel chart recorder (Chessel). The time of each analgesic demand was recorded automatically on the chart recorder. These recordings were subsequently analysed for average respiratory frequency, end tidal carbon dioxide concentration and the incidence of apnoea that lasted for longer than 10 seconds.

Patients were visited 3 and 6 hours after operation for assessment of conscious state and questioned as to their degree of pain and nausea. Patients were again visited at 24 hours and asked to mark 10-cm linear analogues¹² representing overall pain, pain at rest, pain on movement, nausea, mood, amnesia and dizziness. The Palliator was then removed and an intramuscular analgesic prescribed.

Respiratory rates and end tidal carbon dioxide levels were averaged for each patient over the 24-hour period and compared using the Mann-Whitney *U*-test. The incidence of respiratory apnoea and the visual analogue scores were also compared by means of the Mann-Whitney *U*-test. Qualitative data were analysed by the Fisher exact probability test.

Results

Eleven patients received pethidine alone and 13 received pethidine with doxapram. The age and weight distribution (Table 1) was similar for both groups, although by chance there was a higher ratio of women in the group who received pethidine alone.

There was no difference in consumption of pethidine between the two groups of patients (Table 2). The mean dose of doxapram given to patients in the relevant group was 730 mg (Table 2). No adverse effect of the initial loading dose given in the recovery ward was observed. Mean linear analogue scores are shown in Table 3. Overall pain was scored higher in patients who received doxapram ($p < 0.05$). However, this was not consistent since pain at rest was less ($p < 0.1$) and pain on movement was scored similarly by both groups. Drowsiness and amnesia for postoperative events were scored higher by patients who received doxapram ($p < 0.1$). There were no differences in subjective assessments of dizziness, nausea or mood. There were also no differences between the groups in the objective observations of physical and conscious state made 3 and 6 hours postoperatively. Antiemetic requirements during the 24-hour period were similar (Table 2).

Respiratory monitoring revealed a slightly higher mean respiratory rate and lower mean end tidal carbon dioxide concentration in patients who received doxapram (Table 4). The total incidence of respiratory apnoeas that lasted

Table 4. Mean respiratory rate, end tidal carbon dioxide and incidence of apnoea in pethidine and pethidine + doxapram groups.

	Pethidine alone (n = 11)	Pethidine + doxapram (n = 13)	Significance
Mean (range) respiratory rate, breaths/minute	17.2 (11.6–24.2)	18.7 (13.2–25.7)	NS
Mean (range) end tidal CO ₂ , kPa	5.8 (5.1–6.7)	5.5 (4.7–7.1)	NS
Total number of apnoeas			
lasting 10–15 seconds	73	99	NS
lasting > 15 seconds	82	21	p < 0.1
Number of patients with apnoea			
lasting 10–15 seconds	7	10	NS
lasting > 15 seconds	9	6	p < 0.1

NS, p > 0.1.

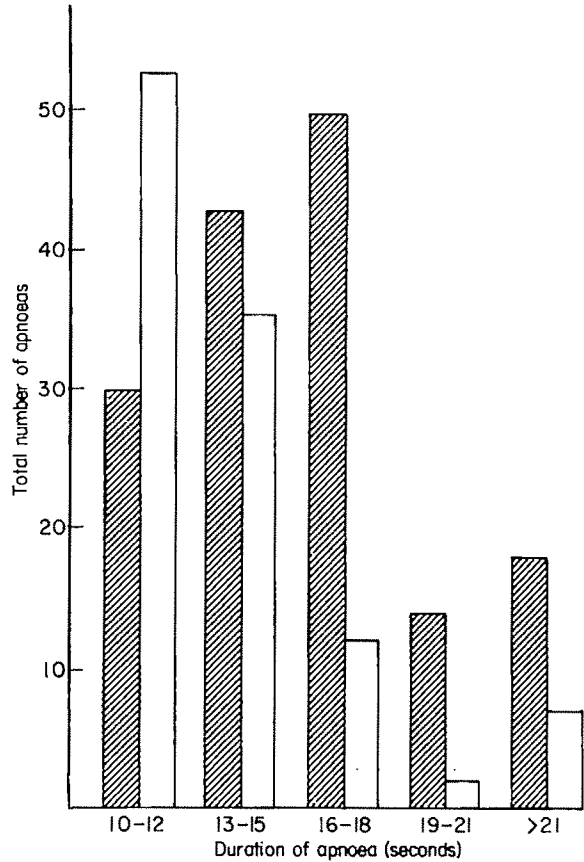


Fig. 1. Distribution of apnoea in patients who received pethidine alone (■) or pethidine + doxapram (□).

longer than 10 seconds was similar in the two groups but there were fewer apnoeic episodes that lasted more than 15 seconds in patients who received doxapram ($p < 0.1$). The variation in the distribution of apnoeas of different duration is shown in Fig. 1.

Discussion

There was only a small increase in mean respiratory frequency and a small decrease in end tidal carbon dioxide concentration in patients who received doxapram. This is at variance with other workers who found an increase in respiratory rate,¹³ minute volume⁸ and decrease in P_{aCO_2} ¹⁴ after short infusions of doxapram. However, doxapram has

a short half-life and plasma levels decline rapidly after a short infusion;¹⁵ therefore, the effects of our intermittent doses may have been too short-lived to have much effect on the mean values of respiratory frequency and end tidal carbon dioxide over a 24-hour period. Moreover, the average dose of doxapram administered in this study was approximately 30 mg/hour. Nevertheless, this is in the order of the lowest infusion rate (0.5–4.0 mg/kg) for the treatment of respiratory depression. A higher ratio of doxapram to pethidine might perhaps have given less depression of respiration.

The incidence of postoperative respiratory apnoea in patients who received intravenous opioid analgesia is similar to our previous findings (in press) and that of other workers.² Doxapram did not reduce the total incidence of apnoea but there was some protection from apnoea of longer duration. This is of interest because long apnoeic periods are more likely to be associated with hypoxaemia and are hence more hazardous. A continuous intravenous infusion of doxapram is useful in protecting premature infants from idiopathic apnoea¹⁶ but such apnoea may be of different aetiology to those encountered in adults during recovery from surgery. Furthermore, the intermittent dose of doxapram administered in this study may have afforded only short periods of protection against the more prolonged respiratory effects of pethidine.

Doxapram has an uncertain effect in the antagonism of opioid analgesia. Several workers have demonstrated little effect on opioid analgesia at doses that effectively antagonise respiratory effects.^{13,17} Others have found that doxapram does antagonise morphine analgesia,⁸ with increased morphine requirements.⁹ There was no increase in demand for pethidine in this study but pain score was reported as greater in the doxapram group. This could not be related to decreased sedation because patients who received doxapram scored sedation higher than the control group. If the quality of analgesia is reduced, this limits the possibility of increasing the ratio of doxapram to pethidine delivered in order to diminish respiratory depression.

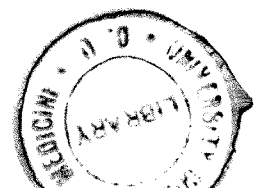
There is theoretical advantage in the administration by PCA of a respiratory stimulant such as doxapram simultaneously with pethidine but the difference in duration of action of the two drugs probably provides only partial antagonism. The possible beneficial effect of decreasing the duration of apnoeic periods when they occur merits further investigation, even though an increased dose of doxapram could have a deleterious effect upon the quality of analgesia.

Acknowledgments

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References

1. CATLING JA, PINTO DM, JORDAN C, JONES JG. Respiratory effects of analgesia after cholecystectomy: comparison of continuous and intermittent papaveretum. *British Medical Journal* 1980; **281**: 478-80.
2. CATLEY DM, THORNTON C, JORDAN C, LEHANE JR, ROYSTON D, JONES JG. Pronounced, episodic oxygen desaturation in the postoperative period: its association with ventilatory pattern and analgesic regimen. *Anesthesiology* 1985; **63**: 20-8.
3. CATLEY DM, THORNTON C, JORDAN C, ROYSTON D, LEHANE JR, JONES JG. Continuous respiratory monitoring reveals oxygen desaturation with paradoxical respiration. *American Review of Respiratory Disease* 1982; **125**: S105.
4. JONES JG, JORDAN C, SCUDDER C, ROCKE DA, BARROWCLIFFE M. Episodic postoperative oxygen desaturation: the value of added oxygen. *Journal of the Royal Society of Medicine* 1985; **78**: 1019-22.
5. HIRSH K, WANG SC. Selective respiratory stimulating action of doxapram compared to pentylenetetrazol. *Journal of Pharmacological and Experimental Therapeutics* 1974; **189**: 1-11.
6. MITCHELL RA, HERBERT DA. Potencies of doxapram and hypoxia in stimulating carotid-body chemoreceptors and ventilation in anesthetized cats. *Anesthesiology* 1975; **42**: 559-66.
7. LEES NW, HOWIE HB, MELLON A, MCKEE AH, MCDIARMID IA. The influence of doxapram on postoperative pulmonary function in patients undergoing upper abdominal surgery. *British Journal of Anaesthesia* 1976; **48**: 1197-1200.
8. GUPTA PK, DUNDEE JW. Morphine combined with doxapram or naloxone. A study of postoperative pain relief. *Anaesthesia* 1974; **29**: 33-9.
9. GAWLEY TH, DUNDEE JW, GUPTA PK, JONES CJ. Role of doxapram in reducing pulmonary complications after major surgery. *British Medical Journal* 1976; **1**: 122-4.
10. STEELE RJC, WALKER WS, IRVINE MKA, LEE D, TAYLOR TV. The use of doxapram in the prevention of postoperative pulmonary complications. *Surgery, Gynecology and Obstetrics* 1982; **154**: 510-2.
11. ROSEN M, WILLIAMS B. The valved-Y-Cardiff connector (V.Y.C. Con). *Anaesthesia* 1979; **34**: 882-4.
12. REVILL SI, ROBINSON JO, ROSEN M, HOGG MIJ. The reliability of a linear analogue scale for evaluating pain. *Anaesthesia* 1976; **31**: 1191-8.
13. GAIROLA RL, GUPTA PK, PANDLEY K. Antagonists of morphine-induced respiratory depression. A study in post-operative patients. *Anaesthesia* 1980; **35**: 17-21.
14. DOWNING JW, JEAL DE, ALLEN PJ, BULEY R. I.V. doxapram hydrochloride and pulmonary complications after lower abdominal surgery. *British Journal of Anaesthesia* 1977; **49**: 473-7.
15. ROBSON RH, PRESCOTT LF. A pharmacokinetic study of doxapram in patients and volunteers. *British Journal of Clinical Pharmacology* 1979; **7**: 81-7.
16. BARRINGTON KJ, FINER NN, PETERS KL, BARTON J. Physiologic effects of doxapram in idiopathic apnoea of prematurity. *Journal of Pediatrics* 1986; **108**: 124-9.
17. DUNDEE JW, GUPTA PK, JONES CJ. Modification of the analgesic action of pethidine and morphine by three opiate antagonists, a respiratory stimulant (doxapram), and an analeptic (nikethamide); a study using an experimental pain stimulus in man. *British Journal of Pharmacology* 1973; **48**: 326P.



A comparison of nalbuphine with fentanyl for postoperative pain relief following termination of pregnancy under day care anaesthesia

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Summary

A double-blind investigation was undertaken to compare the efficacy of nalbuphine and fentanyl in the prevention of pain after day case termination of pregnancy. Forty patients were allocated randomly to receive nalbuphine 0.25 mg/kg or fentanyl 1.5 µg/kg immediately before induction of anaesthesia. The patients completed scores for pain and nausea, and performed a reaction time test to assess recovery. An observer assessed patient appearance at 1, 2 and 4 hours postoperatively. Patients who received nalbuphine had significantly lower pain scores at 1 hour ($p < 0.01$) and 2 hours ($p < 0.05$) and required significantly ($p < 0.05$) less postoperative analgesia. No significant differences were found between the groups for incidence of nausea or for observer assessment of appearance. There was some evidence of psychomotor impairment at 2 hours in the nalbuphine group. Freedom from Controlled Drug Act regulations and improved analgesia with nalbuphine, render it more satisfactory for day case surgery than the more commonly used fentanyl.

Key words

Anaesthesia; outpatient.

Analgesics, narcotic; fentanyl, nalbuphine.

Approximately 150 000 terminations of pregnancy are performed annually in England and Wales. Eighty-five percent of procedures are vacuum aspirations performed under general anaesthesia at less than 14 weeks' gestation. Day case surgery offers efficient use of manpower and facilities and is preferred by many patients, yet in 1982 less than 30% were performed in this way. Several anaesthetic techniques have been described for day case surgery^{1–3} but none is ideal.

Day case surgery requires adequate depth of anaesthesia with rapid recovery. The treatment of postoperative pain is frequently forfeited to achieve this. Collins *et al.*¹ observed moderate to severe pain in 36% of patients following termination of pregnancy and 48% required postoperative analgesia. Hackett *et al.*² noted in a similar study that approximately 30% of patients complained of moderate to severe pain and 42% required analgesia.

Many techniques have been described that use the shorter-acting opioids fentanyl and alfentanil for termination of pregnancy^{1–6} but these drugs offer little pain relief in the recovery period. Nalbuphine is a partial kappa agonist/mu antagonist opioid of the phenanthrene series which was synthesised in an attempt to produce analgesia without the

undesirable side effects of a mu agonist, notably respiratory depression and drug dependence. It has been demonstrated to exhibit a ceiling effect to both respiratory depression and analgesia,^{7,8} with a lower incidence of nausea and vomiting than morphine,⁹ but has nevertheless been shown by some observers to provide satisfactory postoperative analgesia following abdominal and orthopaedic surgery.^{10–12}

The pharmacological profile of nalbuphine and its freedom from control by the *Misuse of Drugs Act* would appear to be useful properties in an analgesic for day case surgery. Fentanyl is one of the more commonly used analgesics in this situation and we therefore undertook a double-blind comparison of analgesia and recovery following anaesthesia with either nalbuphine or fentanyl in patients who underwent day case surgery.

Methods

The investigation was approved by the District Ethics Committee. Forty patients (age range 16–40 years) were studied following surgery for termination of pregnancy up to 12 weeks' gestation. Informed consent was obtained from the patients who were allocated randomly to receive either nal-

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buphine 0.25 mg/kg or fentanyl 1.5 µg/kg intra-operatively. Patients with a history of asthma, drug allergy or sensitivity to opioids were excluded from the study.

No premedication was administered and the patients were fasted for at least 8 hours. The selected opioid was given intravenously in the anaesthetic room and anaesthesia was induced one minute later with thiopentone 3–4 mg/kg, and maintained conventionally using a Bain breathing system with 66% nitrous oxide in oxygen supplemented with enflurane according to the clinical judgment of the anaesthetist. Syntocinon 10 units was administered intravenously at the onset of cervical dilatation. The duration of surgery and anaesthesia and any untoward events were recorded.

Observations in the recovery room were made by the nursing staff, who were unaware of the anaesthetic technique employed. Recovery of consciousness was assessed as the time the patient could correctly give her name, date of birth and address. Postoperative analgesia was prescribed as paracetamol 1 g orally 6 hourly.

The patients were assessed by a single trained observer (blinded to the anaesthetic technique) on four separate occasions, pre-operatively and 1, 2 and 4 hours postoperatively. The patient's appearance was recorded as asleep, awake and calm, or awake and restless. The patients also completed a 10-cm horizontal linear analogue scale for pain, as described elsewhere.¹³ The presence of nausea was scored by the patient as no nausea (0), slight nausea (1), moderate/severe nausea (2) or vomiting (3). The consumption of postoperative analgesics was recorded.

Recovery from anaesthesia was assessed by measurement of psychomotor function using a reaction timer. This is an automated, hand-held instrument for recording simple visuomotor reaction times. In essence, the device generates a light at randomly timed intervals at a frequency of approximately 20 per minute. The light is extinguished by the depression of a button and the time interval to achieve this (in milliseconds) is displayed on an LED. Following practice sessions to establish a steady baseline, the reaction times were recorded at each assessment postoperatively. The patient operated the device for approximately one minute on each occasion and a mean value of approximately 20 reaction times was computed automatically.

Statistical analysis of the data was undertaken using the unpaired Student's *t*-test for demographic data, the Wilcoxon rank sum test for linear analogue scores and the Chi-

squared test with Yates' correction, for observer assessments and patient scores for nausea.

Results

The two groups of patients were similar with respect to age, weight, ASA status and previous anaesthetic experience (Table 1). There were no significant differences in gestational age, dose of anaesthetic agent, the duration of anaesthesia or time to recovery following completion of surgery (Table 2).

Table 1. Demography of patients, expressed as mean (SEM).

	Nalbuphine (n = 20)	Fentanyl (n = 20)
Age, years	24.1 (1.7)	22.7 (1.4)
Weight, kg	60.2 (2.5)	57.1 (1.0)
ASA grade 1	19	19
grade 2	1	1
Number of patients with previous anaesthetic	7	6

Table 2. Gestational age, duration of anaesthesia, recovery time and dose of anaesthetic drugs in the two groups of patients, expressed as mean (SEM).

	Nalbuphine (n = 20)	Fentanyl (n = 20)
Gestation, weeks	9.9 (0.4)	10.2 (0.3)
Cervical dilatation, mm	9.9 (0.2)	9.7 (0.2)
Duration of anaesthesia, minutes	11.4 (1.2)	12.5 (1.1)
Recovery time, minutes	8.3 (1.1)	9.5 (1.4)
Dose of thiopentone, mg/kg	4.6 (0.2)	4.6 (0.2)
Maximum concentration of enflurane administered, %	2.5 (0.2)	2.6 (0.2)

There was significantly less pain postoperatively in the nalbuphine group at 1 hour ($p < 0.01$) and at 2 hours ($p < 0.05$) (Fig. 1). Eight patients (40%) in the nalbuphine group scored no pain at 1 hour, compared with two (10%) in the fentanyl group. The numbers with no pain were 10 (50%) and 4 (20%), respectively, at 2 hours postoperatively. However, there was no difference between the groups at 4 hours. Nine patients (45%) in the fentanyl group required postoperative analgesia with paracetamol 1 g at a mean

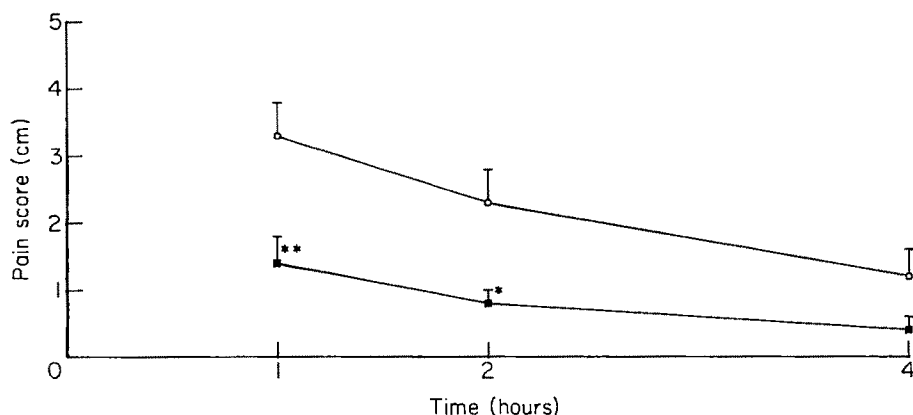


Fig. 1. Graph of mean pain scores, with time. ■, Nalbuphine; ○, fentanyl; bars indicate SEM. * $p < 0.05$; ** $p < 0.01$.

time of 1.47 hours (SEM 0.16) following recovery. This was significantly greater ($p < 0.05$) than in the nalbuphine group, where two patients (10%) received paracetamol 1 g at a mean time of 2.6 hours (SEM 0.04) after recovery.

There were no significant differences between the observed appearances of the two groups at any time postoperatively (Table 3) or between the scores for nausea (Table 4).

The baseline reaction time was similar for both groups pre-operatively (Table 5). Both groups showed increases in reaction time postoperatively but there was no significant difference between the groups. Table 6 shows the mean

Table 3. Appearance of patient, expressed as number of patients at 1, 2 and 4 hours postoperatively.

	Nalbuphine (n = 20)	Fentanyl (n = 20)
1 hour		
Asleep	4	4
Awake and calm	14	13
Awake and restless	2	3
2 hours		
Asleep	3	1
Awake and calm	17	19
Awake and restless	0	0
4 hours		
Asleep	1	1
Awake and calm	18	19
Awake and restless	1	0

Table 4. Subject scoring of nausea on a scale of 1–3, expressed as mean (SEM).

	1 hour	2 hours	4 hours
Nalbuphine	0.2 (0.14)	0.7 (0.30)	0.4 (0.23)
Fentanyl	0.9 (0.37)	0.5 (0.21)	0.2 (0.11)

Table 5. Mean (SEM) raw scores of reaction times, milliseconds.

	Baseline	1 hour	2 hours	4 hours
Nalbuphine	237.3 (6.6)	293.4 (11.4)	265.4 (11.5)	248.9 (9.9)
Fentanyl	243.6 (7.0)	270.3 (8.3)	253.8 (6.8)	242.7 (5.8)

Table 6. Mean percentage differences in reaction times from control (= 100%).

	1 hour	2 hours	4 hours
Nalbuphine	+23.7*	+11.9*	+0.43
Fentanyl	+11.1*	+4.2	−0.4

* $p < 0.05$.

percentage change from baseline in the two groups. The reaction times at 1 hour in both groups were significantly greater ($p < 0.05$) than baseline, and at 2 hours the nalbuphine group had a significantly greater ($p < 0.05$) reaction time compared with baseline.

Discussion

This study of the use of nalbuphine or fentanyl for outpatient termination of pregnancy shows that nalbuphine was associated with significantly less pain, but there was no difference in sedation or nausea from 1–4 hours after

recovery from anaesthesia. It is axiomatic that adequate analgesia should be provided during and after recovery from painful surgery. In addition rapid recovery is important in a day stay unit, to ensure that patients' protective reflexes are present as soon as possible, and to allow prompt discharge home. Several anaesthetic techniques have been described for termination of pregnancy but no single method meets all the requirements.

Collins *et al.*¹ compared inhalational anaesthesia using halothane with a technique using alfentanil in unpremedicated patients. The incidence of postoperative moderate to severe pain was not significantly different between the groups; it was 36% in the halothane group and 27% in the alfentanil group. Over 40% of all patients required postoperative analgesia. Another study² compared techniques using fentanyl and enflurane in unpremedicated patients. The frequency of moderate to severe pain was similar in both groups, approximately 28%, and there was no difference in postoperative analgesic requirements. Clearly, termination of pregnancy is associated with an appreciable incidence of pain postoperatively, and the use of short-acting opioids intra-operatively provides little postoperative pain relief. Our findings confirm this, since there was a higher incidence of pain in the fentanyl group and 45% required postoperative analgesia. However, only 10% of patients in the nalbuphine group required postoperative analgesia and the pain scores at 1 and 2 hours were significantly less than in the fentanyl group.

The use of a longer-acting opioid, such as nalbuphine, with a half-life of approximately 4 hours,⁹ may be expected to lengthen recovery time. However, we found that the recovery time was not significantly different from the fentanyl group. There was also no significant difference in observer assessments of appearance. Using a sensitive test of psychomotor performance in the form of a reaction time, however, we observed significant impairment in the nalbuphine group for up to 2 hours postoperatively but only for 1 hour in the fentanyl group. Direct comparison is not possible between results obtained in different studies but recovery times similar to the present ones were reported with halothane,¹ enflurane² and fentanyl.² The use of alfentanil, however, has been shown to provide more rapid recovery.¹

Nausea and vomiting are a common problem with termination of pregnancy and may be associated with the emotional state of the patient, the oxytocic agent used and the anaesthetic technique. Incidences of 24%,² 30%¹ and 55%³ have been reported with anaesthetic techniques using short-acting opioids. These are significantly greater than with inhalational techniques, where incidences of 8%² and 9%¹ have been reported. In the present study, 25% of all patients experienced some degree of nausea during the 4-hour postoperative period and there was no inter-group difference. This is comparable to the other studies using opioids.

Enflurane was employed during the maintenance period in the present study. It is particularly suitable for outpatient anaesthesia because of its ease of administration and relatively low frequency of side effects. Induction and recovery are significantly faster than with halothane.¹⁴ Enflurane may lead to an increase in blood loss during termination of pregnancy,² but in low doses (inspired concentration < 1%) it has been shown not to increase blood loss in comparison with an opioid anaesthetic.⁶ Enflurane reached a maximum inspired concentration of approximately 2.5% in both

groups in the present study, but was considerably less for the majority of anaesthetic time.

Nalbuphine has been shown to provide adequate post-operative pain relief.¹⁰⁻¹² It has some advantages over pure agonists, with a proven maximum respiratory depressant effect.^{7,8} Because of the relatively flat dose-response curve, the dose is less critical than for other opioids, for example morphine.¹⁵ Its analgesic potency appears to be similar to that of morphine¹⁶ and the dose used in this study was within the recommended range. Fentanyl 200 µg is equipotent to morphine 10 mg;¹⁷ however, we selected the dose of fentanyl as that used most commonly in similar studies.^{2,3,6} Nalbuphine is not subject to the restrictions of the *Misuse of Drugs Act* and therefore it is readily available in peripheral units.

In summary, pain is a common problem after day case surgery for termination of pregnancy. We found an incidence of pain with fentanyl similar to that described by other workers using this drug. Nalbuphine produces a significant reduction in the incidence of pain in the first 2 hours after termination compared to fentanyl and does not increase recovery time or the incidence of nausea. There is some evidence of psychomotor impairment up to 2 hours post-operatively. Freedom from *Controlled Drug Act* regulations and improved analgesia render it more suitable for day case surgery than the more commonly used fentanyl.

References

1. COLLINS KM, PLANTEVIN OM, WHITBURN RH, DOYLE JP. Outpatient termination of pregnancy: halothane or alfentanil-supplemented anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 1226-31.
2. HACKETT GH, HARRIS MNE, PLANTEVIN OM, PRINGLE HM, GARRIOCH DB, AVERY AJ. Anaesthesia for outpatient termination of pregnancy. *British Journal of Anaesthesia* 1982; **54**: 865-70.
3. OGG TW, JENNINGS RA, MORRISON CG. Day-case anaesthesia for termination of pregnancy. Evaluation of a total intravenous *Anaesthesia*, 1987; **59**: 929P-30P.
4. WEST SL, MOORE CA, GILLARD M, BROWNE PD. Anaesthesia for suction termination of pregnancy. *Anaesthesia* 1985; **40**: 669-72.
5. CUNDY JM, SCOTT WE. Sequential use of thiopentone and etomidate in anaesthesia for termination of pregnancy. *Anaesthesia* 1983; **38**: 155-8.
6. SIDHU MS, CULLEN BF. Low-dose enflurane does not increase blood loss during therapeutic abortion. *Anesthesiology* 1982; **57**: 127-9.
7. ROMAGNOLI A, KEATS AS. Ceiling effect for respiratory depression by nalbuphine. *Clinical Pharmacology and Therapeutics* 1980; **27**: 478-85.
8. PUGH GC, BROWN DT, DRUMMOND GB. The effects of nalbuphine hydrochloride and naloxone on the ventilatory response to carbon dioxide in volunteers. *British Journal of Anaesthesia*, 1987; **59**: 929 P-30P.
9. FRAGEN JR, CALDWELL N. Acute intravenous premedication with nalbuphine. *Anesthesia and Analgesia* 1977; **56**: 808-12.
10. BAHAR M, ROSEN M, VICKERS MD. Self-administered nalbuphine, morphine and pethidine. Comparison, by intravenous route, following cholecystectomy. *Anaesthesia* 1985; **40**: 529-32.
11. TAMMISTO T, TIGERSTEDT I. Comparison of the analgesic effects of intravenous nalbuphine and pentazocine in patients with postoperative pain. *Acta Anaesthesiologica Scandinavica* 1977; **21**: 390-4.
12. BROCK-UTNE JG, RITCHIE P, DOWNING JW. A comparison of nalbuphine and pethidine for post-operative pain relief after orthopaedic surgery. *South African Medical Journal* 1985; **68**: 391-3.
13. REVILL SI, ROBINSON JO, ROSEN M, HOGG MIJ. The reliability of a linear analogue for evaluating pain. *Anaesthesia* 1976; **31**: 1191-8.
14. GOVAERTS MJM, SAUNDERS M. Induction and recovery with enflurane and halothane in paediatric anaesthesia. *British Journal of Anaesthesia* 1975; **47**: 877-80.
15. KRISHNAN A, TOLHURST-CLEAVER CL, KAY B. Controlled comparison of nalbuphine and morphine for post-tonsillectomy pain. *Anaesthesia* 1985; **40**: 1178-81.
16. BEAVER WT, FEISE GA. A comparison of analgesic effect of intramuscular nalbuphine and morphine in patients with post-operative pain. *Journal of Pharmacology and Experimental Therapeutics* 1978; **204**: 487-96.
17. VICKERS MD, SCHNIEDEN A, WOOD-SMITH FG. *Drugs in anaesthetic practice*, 6th edn. London: Butterworths, 1984.

Pain-free injection in infants

Use of a lignocaine–prilocaine cream to prevent pain at intravenous induction of general anaesthesia in 1–5-year-old children

C. S. HOPKINS, C. J. BUCKLEY AND G. H. BUSH

Summary

A randomised, placebo-controlled, double-blind study was undertaken in 111 children between the ages of 1 and 5 years to assess the efficacy of EMLA 5% cream in the alleviation of venepuncture pain at intravenous induction of general anaesthesia using 27-gauge needles. Pain assessment was made by an operating department assistant using both verbal rating scale and visual analogue scale methods. Seventy-five children, of whom 24 were premedicated, were treated with EMLA cream and 36 with placebo, 14 of whom were premedicated. Significantly lower pain scores were recorded in the children treated with EMLA cream (verbal rating scale: premedicated $p < 0.05$, unpremedicated $p < 0.001$; visual analogue scale: premedicated $p < 0.0005$, unpremedicated $p < 0.0002$). No variation in analgesia was found for application times between 30 and 300 minutes and there were no serious side effects.

Key words

Anaesthetics, local; prilocaine, lignocaine.

Anaesthetic techniques, regional; topical.

Fear and pain can make the insertion of intravenous needles in children a traumatic experience. Intravenous induction of general anaesthesia in paediatric practice, even by experienced paediatric anaesthetists, may produce severe distress and lead to the development of 'needle-phobia', especially if the child requires subsequent repeat surgery. This problem is not solved completely by the use of fine needles (e.g. 27-gauge) or by the administration of opioid premedication. Day case paediatric patients pose particular problems.

The local anaesthetic cream EMLA (eutectic mixture of local anaesthetics), which contains a mixture of lignocaine and prilocaine, has been shown to produce dermal analgesia before skin puncture and other superficial skin procedures. More than 500 adults and children have been treated to date with EMLA in controlled clinical trials and the local anaesthetic properties of the cream established.^{1–4} These studies have concerned mainly pain on venepuncture, and EMLA was granted a product licence for venepuncture in Sweden in November 1984 and in the United Kingdom in January 1986. Local adverse reactions are transient and disappear without treatment.

There have to date been no double-blind studies on the use of EMLA in children under 4 years of age. Children

between the ages of 1 and 4 years in our experience constitute a considerable proportion of patients who present for day case surgical procedures, as well as repeat or staged treatment for burns and plastic surgery. An unpleasant intravenous induction due to venepuncture pain can make subsequent attempts frightening for the child and technically difficult for the anaesthetist.

Previous studies have identified a minimum application period of 60 minutes to be necessary to ensure the least amount of pain in children in the 4–17 years age group.⁵ Adult studies have identified a 45-minute minimum application period.⁶ The objectives of this study were to examine the efficacy of EMLA with respect to alleviation of venepuncture pain at intravenous induction of general anaesthesia in children aged 1–5 years, to identify the optimal application time and to evaluate possible adverse reactions to the preparation.

Methods

One hundred and twenty children between the ages of 1 and 5 years who presented at Alder Hey Children's Hospital for day case surgery under general anaesthesia were included in the study. The study protocol was approved by

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Table 1. Comparison of EMLA and placebo treatment groups.

	EMLA group (<i>n</i> = 75)	Placebo group (<i>n</i> = 36)
Age, years		
Mean (SD)	3.7 (1.29)	4.3 (1.32)
Median (range)	4 (1–6)	5 (1–6)
Weight, kg		
Mean (SD)	15.6 (2.89)	17.1 (3.86)
Median (range)	15 (8–21)	18 (10–26)
Sex, M:F	55:20	26:10

the hospital ethical committee, and informed, written consent obtained from parents.

EMLA 5% consists of a mixture of lignocaine base 25 mg/ml (107 mmol/litre) and prilocaine base 25 mg/ml (113 mmol/litre). The remaining ingredients are an emulsifier Arlatone® 289, a viscosity-increasing agent Carbopol® 934, and water. The pH of the cream is adjusted to 9.4 with sodium hydroxide. One gramme of the cream corresponds to approximately 1 ml. The eutectic mixture of local anaesthetics was substituted with Miglycol® 812 oil in the placebo cream. The two formulations are visually and cosmetically identical. EMLA and placebo were packed in identical aluminium tubes marked with trial number and patient number.

The study involved a double-blind comparison of EMLA cream with placebo; 80 children received EMLA and 40 received placebo. The placebo treatments were distributed at random across the 120 samples. According to the practice of the consultant anaesthetist responsible for the particular list, the patients received either no premedication or a mixture of mefenamic acid 8.3 mg/ml, trimeprazine 1.0 mg/ml and atropine 30 µg/ml in a dose of 1.0 ml/kg up to a maximum of 30 ml one hour pre-operatively.

One tube of cream was used to apply a thick layer over the dorsum of each hand at least 30 minutes prior to each operating list. The cream was covered with a Tegaderm® (3M) occlusive dressing as supplied routinely with EMLA. All patients for a particular operating list were treated together in this way. A note was made of the tube number used and of the application time. An assessment of the emotional state of the child was made on arrival in the anaesthetic room, using a 100-mm visual analogue scale (VAS) with a range from 'asleep' to 'agitated'.

The occlusive dressings were removed, the time noted and the cream wiped off using a dry swab. Any oedema, erythema or blanching were noted and recorded on a four-point scale: none, slight, moderate or severe. The anaesthetist performed venepuncture using a 27-gauge needle. The operating department assistant who held the child's arm was required to make two assessments of the child's reaction at the moment of venepuncture. The first used a category verbal rating scale (VRS) with the following four categories: no reaction, no whimpering, no grimacing or reflex movement; slight pain, slight whimpering, grimacing, minor reflex movement; moderate pain, continual whimpering, grimacing, reflex movement; severe pain, loud crying, intense reflex movement. A 100-mm visual analogue scale (VAS) was also used; the left edge indicated 'no pain' and the right edge, 'severe pain'. The anaesthetist who performed venepuncture recorded the degree of difficulty

on a four-category verbal rating scale: not used, easy, difficult or impossible.

The visual analogue scale data for response to venepuncture were tested by the Wilcoxon rank sum test with the group split into those who received analgesic premedication and those who did not. The verbal rating scale results were tested using the Chi-square test. A correlation matrix including the variables application time, condition on arrival in theatre and visual analogue score, was also drawn up for those patients who received EMLA and no premedication.

Results

Results from 111 patients were analysed. The results of nine patients were excluded because surgery was rescheduled after treatment with EMLA. No patient's results were excluded because of adverse reaction to EMLA. Demographic data are given in Table 1.

Twenty-four of the 75 patients who received EMLA (32%) received premedication as did 14 of the 36 patients in the placebo group (39%). There was no statistical difference between those patients who received either premedication or no premedication, in terms of condition on arrival in theatre as assessed by visual analogue scale comparison of the EMLA group to the placebo group; however, there was a statistically significant difference within each group between those who were premedicated and those who were not ($p < 0.01$). This difference is also seen in the visual analogue scale and verbal rating scale assessments of pain on venepuncture, with lower scores for the premedicated subgroup.

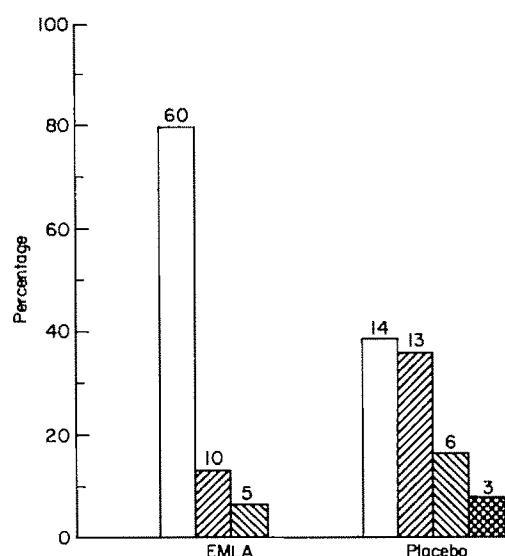


Fig. 1. Comparison of verbal rating scale pain scores for all patients, EMLA treated versus placebo treated. Chi-square analysis shows a significantly greater incidence of low pain (none, slight) in subjects treated with EMLA ($\chi^2 = 20.96$, d.f. = 3, $p < 0.001$). Pain scores: □, none; ▨, slight; ▩, moderate; ■, severe.

Figure 1 compares the verbal rating scale for pain of the EMLA group with the placebo group for all patients. Treatment with EMLA resulted in significantly less subjectively assessed pain on venepuncture ($\chi^2 = 20.96$, d.f. = 3, $p < 0.001$). Separate analysis of premedicated and unpremedicated subgroups also revealed a similar reduction in assessed

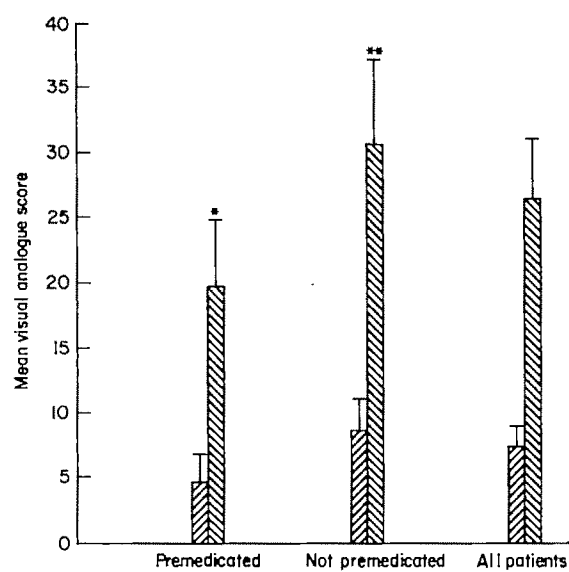


Fig. 2. Mean (SEM) visual analogue scale scores for EMLA and placebo groups subdivided into premedicated and unpremedicated subgroups. Wilcoxon rank sum test shows significantly lower mean scores for EMLA treated groups (* $p < 0.0005$, ** $p < 0.0002$). ▨, EMLA group; ▩, placebo group.

pain (premedicated, $\chi^2 = 4.77$, $p < 0.05$; unpremedicated, $\chi^2 = 14.88$, $p < 0.001$).

Figure 2 shows the mean visual analogue scale scores for the EMLA and placebo groups. Analysis of the premedicated and unpremedicated subgroups using the Wilcoxon-Rank sum test indicates significantly lower scores for patients who received EMLA in both subgroups (premedicated, $w = 387.5$, $p < 0.0005$; unpremedicated, $w = 1120$, $p < 0.0002$). Figures 3 and 4 illustrate the individual visual

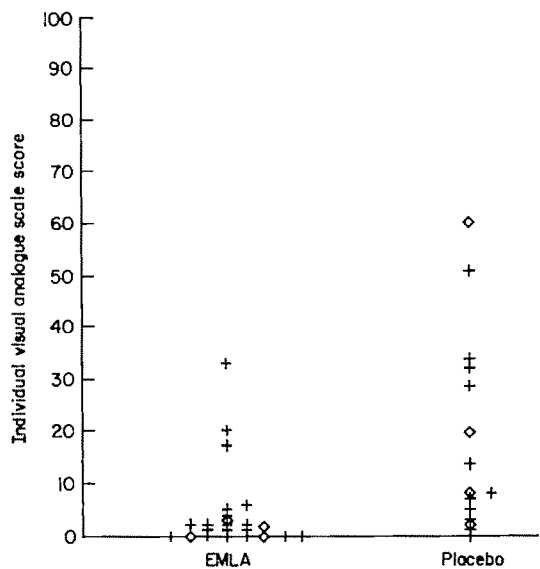


Fig. 3. Individual visual analogue scale scores for premedicated subgroup, and condition on arrival in anaesthetic room. Wilcoxon rank sum test shows significantly lower scores for EMLA treated group ($p < 0.0005$). +, Calm; ◇, agitated.

analogue scale scores for the premedicated and unpremedicated subgroups. The patient's condition on arrival in the anaesthetic room is also shown, according to the visual analogue scale score for this variable.

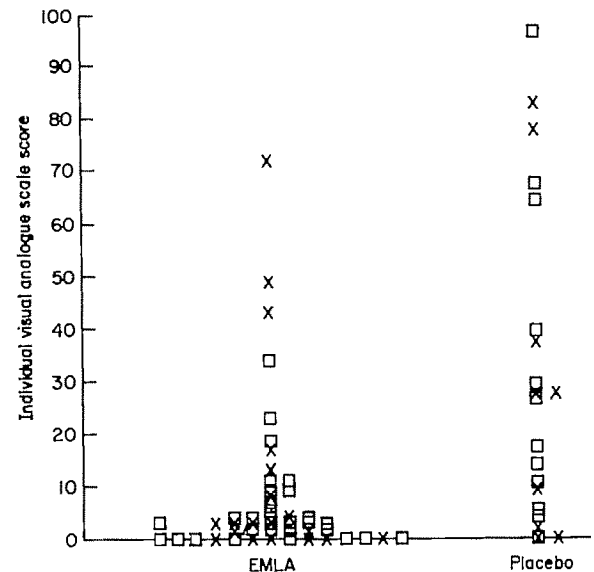


Fig. 4. Individual visual analogue scale scores for unpremedicated subgroup, and condition on arrival in anaesthetic room. Wilcoxon sum test shows significantly lower scores for EMLA treated group ($p < 0.0002$). □, Calm; x, agitated.

Table 2. Correlation matrix between condition on arrival in anaesthetic room, visual analogue scale pain score (VAS) and total application time for 51 unpremedicated patients who received EMLA cream.

	Condition	VAS	Application time
Condition	1.0000 (NS)	0.1219 ($p = 0.197$)	0.1042 ($p = 0.233$)
VAS	0.1219 ($p = 0.197$)	1.0000 (NS)	0.0386 ($p = 0.394$)
Application time	0.1042 ($p = 0.233$)	0.0386 ($p = 0.394$)	1.0000 (NS)

NS, Not significant.

Analysis of a correlation matrix (Table 2) including the variables application time, condition on arrival and visual analogue scale score, shows that there are no significant correlations among these variables. In particular, there is no correlation between application time and efficacy after an application period of 30 minutes.

No serious side effects were noted and there were no cases of oedema. Redness occurred in four patients treated with EMLA and in no patient treated with placebo: in all cases this disappeared within one hour. The incidence of paleness in the EMLA group was mild, 36 cases and moderate, 6. The corresponding results for the placebo group were mild, 14 and moderate, 1.

Discussion

This study completes the assessment of EMLA cream using placebo controlled double-blind methodology in patients of age 1 year and upward. As expected from previous work, EMLA significantly reduced noxious stimulation due to venepuncture and this can only be to the benefit of both children who undergo intravenous induction of general anaesthesia and anaesthetists, since it is our experience that venepuncture can be performed far more easily if the child does not react to needle insertion.

We observed, unlike a previous study on older children, a significant difference in pain scores (both VAS and VRS) with a lower mean score in patients who received analgesic premedication. A minimum application time of at least 30 minutes is required to obtain effective analgesia in the age group studied. This compares with 60 minutes for the age group 4–17 years and 45 minutes for adults. The fact that pain assessment in this study was by observer estimation and not patient reporting may explain the difference in results, but the use of the same observer to minimise inter-observer variation means that the comparison of EMLA and placebo is valid.

There was no significant alteration in mean pain scores up to application times of 300 minutes, so all patients for a particular operating list may be treated at the same time without concern that analgesia may diminish with time. EMLA did not cause any serious skin reaction despite application times of up to 300 minutes. It is prudent to apply EMLA cream at the same time as administration of premedication, at least one hour pre-operatively. The use of oral premedication obviates the need for intramuscular injections, which to a certain extent negates the advantages of using EMLA.

It is our conclusion that EMLA cream should form part of the pre-operative preparation of every child who is to undergo intravenous induction of general anaesthesia, as well as other procedures such as insertion of intravenous cannulae on the ward or venous blood sampling. It is now the practice at The Royal Liverpool Children's Hospitals for the majority of children to be treated with EMLA prior to such procedures. Nursing staff are extremely willing to

undertake this once they see the effect at induction of anaesthesia in the children they accompany to the operating theatre, and in the ward environment.

Acknowledgments

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References

1. EHRENSTRÖM-REIZ GME, REIZ SLA. EMLA—a eutectic mixture of local anaesthetics for topical anaesthesia. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 596–8.
2. HALLEN B, UPPFELDT A. Does lidocaine–prilocaine cream permit painfree insertion of i.v. catheters in children? *Anesthesiology* 1982; **57**: 340–2.
3. HALLEN B, CARLSSON P, UPPFELDT A. Clinical study of a lignocaine–prilocaine cream to relieve the pain of venepuncture. *British Journal of Anaesthesia* 1985; **57**: 326–8.
4. MAUNUKSELA E-L, KORPELA R. Double-blind evaluation of a lignocaine–prilocaine cream (EMLA) in children. *British Journal of Anaesthesia* 1986; **58**: 1242–5.
5. HALLEN B, OLSSON GL, UPPFELDT A. Pain-free venepuncture. Effect of timing on application of local anaesthetic cream. *Anaesthesia* 1984; **39**: 969–72.
6. EHRENSTROM-REIZ GME, REIZ SLA, STOCKMAN O. Topical anaesthesia with EMLA, a new lidocaine–prilocaine cream and the Cusum technique for detection of minimal application time. *Acta Anaesthesiologica Scandinavica* 1983; **27**: 510–2.

CASE REPORT

Myocardial infarction in the third trimester of pregnancy

M. BEMBRIDGE AND G. LYONS

Summary

A 30-year-old woman developed severe chest pain while out shopping and was admitted to the delivery suite. She was 38 weeks pregnant with her second child. A diagnosis of myocardial infarction was made and cardiac arrest occurred shortly afterwards. She went into spontaneous labour 30 hours later and was delivered vaginally. This report reviews myocardial infarction in pregnancy and considers the clinical management of this patient.

Key words

Pregnancy.

Complications; arrest, cardiac.

Myocardial infarction during pregnancy is rare and was first described in 1921,¹ since when a total of 77 cases have been reported.^{2–5} The *Confidential Enquiries 1979–81*⁶ cites six deaths from coronary artery disease, or a rate of 3.1 per million maternities, a figure which has changed little in a decade.^{7,8} Myocardial infarction in pregnancy is sufficiently rare to prevent a single obstetric anaesthetist from gaining significant experience but it is common enough to occur perhaps once during an individual's working life.

The condition has a high mortality for mother and baby; maternal mortality increases from 0% in the first trimester to 50% in the puerperium. Infant mortality is 40% in the second trimester. A myocardial infarction that occurs in the third trimester has a 21% mortality risk for both mother and baby.²

The patient described here had a proven myocardial infarction in the third trimester, complicated by cardiac arrest; she went into labour spontaneously 30 hours later.

Case history

A 30-year-old woman (gravida 3, para 1) experienced chest pain whilst shopping and was admitted as an emergency to the delivery suite. She still complained of chest pain associated with nausea and dyspnoea when examined. Her pulse rate was 56 beats/minute and arterial blood pressure 80/50 mmHg, with an elevated jugular venous pressure. There were occasional Braxton–Hicks contractions and the fetal heart beat was heard. The initial diagnosis was myocardial ischaemia. She was given diamorphine and prochlorper-

azine while continuous fetal cardiotocography (CTG) was performed and the opinion of the cardiologist sought. A 12-lead ECG performed at this time showed the hyperacute phase of an inferior myocardial infarction, extending laterally. Thereafter her ECG was monitored continuously.

She collapsed suddenly with the cardiac rhythm of ventricular fibrillation whilst these findings were discussed with her. External cardiac massage was started and a DC shock was given immediately. Her rhythm returned to sinus bradycardia which responded to atropine. Lignocaine was required to control ventricular extrasystoles, and the rhythm settled to sinus rhythm with 2nd-degree heart block. An isoprenaline infusion was begun. She recovered consciousness rapidly and stabilised with a pulse rate of 90 beats/minute and arterial pressure of 95/60 mmHg. The fetal CTG showed a marked decrease in rate during the episode of ventricular fibrillation but returned to normal rapidly after resuscitation. The mother was in the wedged position throughout.

She was transferred to the intensive care unit for further therapy and monitoring of central venous pressure, direct intra-arterial pressure, hourly urine output and continuous ECG. She was nursed in a lateral or tilted position at all times. The isoprenaline infusion was gradually withdrawn, to lessen the myocardial oxygen demand, and replaced with dopamine. Oxygen at 40%, ranitidine and diamorphine were also given.

She had three further episodes of chest pain that required analgesia the following day. Her membranes ruptured spontaneously at 23.00 hours, 30 hours after the cardiac

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arrest. On examination the cervix was 1.5 cm dilated, 50% effaced, and membranes were absent. The uterus was contracting 1 in 5 and the fetal heart rate was normal.

A contingency plan for this eventuality had been agreed during discussion between the obstetrician, anaesthetist and cardiologist the day before, and was for an assisted vaginal delivery with continuous lumbar epidural analgesia. The epidural was sited at the L₂-L₃ interspace and 12 ml 0.25% plain bupivacaine in divided doses was given after a test dose of 3 ml 1% plain lignocaine. Six top-ups were required during labour, divided between the right and left lateral positions; they were given before sensation returned.

She achieved full cervical dilatation approximately 4 hours later and was delivered of a 2.58-kg girl by Neville Barnes forceps. Apgar scores were 10 at both 1 and 5 minutes; 10 units of syntocinon were given. The subsequent courses of mother and baby were uneventful. Creatine phosphokinase levels measured on four successive days after infarction are shown in Table 1.

Table 1. Creatine phosphokinase levels post infarction.

Day	Creatine phosphokinase (IU/litre)
1	267
2	3873
3	1498
4	627

Serial ECGs showed the development of a full thickness inferior myocardial infarction that extended laterally. Family history of coronary artery disease was negative and coagulation studies, serum cholesterol and triglycerides, and blood sugar were all normal. However, she was plump and smoked cigarettes. Coronary angiography performed later confirmed the ECG findings and demonstrated a completely occluded right coronary artery but no significant left coronary artery disease. Mother and baby are known to be well at the present.

Discussion

This is the first documented instance of a 38-week pregnancy complicated by cardiac arrest and proceeding to vaginal delivery. Two instances of cardiac arrest that occurred at 4 and 18 weeks' gestation have been reported previously. Both pregnancies continued and were subsequently delivered vaginally.^{4,9}

Cortis *et al.*⁴ made some recommendations about the management of these patients. Firstly, there should be close cooperation between obstetrician and cardiologist when chest or abdominal pain cannot be explained readily. Secondly, coronary angiography should be performed 2-3 months after delivery. Thirdly, predisposing risk factors should be reduced as far as possible. They did not make any recommendations as to the manner of delivery, but Ostheimer and Alper¹⁰ suggest that all these patients should have an elective Caesarean section.

Ginz² reviewed retrospectively 39 cases of myocardial infarction in pregnancy and found that women delivered by Caesarean section suffered 27% mortality and an infant death rate of 9%. On the other hand, those without interference had a 13% maternal and a 27% infant mortality, while those delivered with forceps had neither maternal nor infant mortality.

The decision to manage this patient on the intensive care unit was well considered. Midwives are not trained in recognition of dysrhythmias, and invasive monitoring was not available on the labour ward. Our coronary care unit is distant from the labour ward and operating theatres and is inconvenient for resident obstetric and anaesthetic staff. The intensive care unit is centrally placed and is adjacent to operating theatres staffed 24 hours a day.

Close monitoring was indicated because of cardiovascular instability that required inotropic support. This would have been stopped after 48 hours, had labour not ensued. Pulmonary artery catheterisation was withheld since cardiac output seemed to be adequate. The information derived would have been helpful had this not been the case. This would certainly have been true if hypotension had followed established epidural analgesia. Consideration should therefore be given to pulmonary artery catheterisation when labour is established if the myocardium is known to be significantly compromised.

We elected to use an epidural for labour because of the need for good analgesia and suppression of the expected increase in endogenous catecholamines.¹¹ Experience in the use of epidural analgesia in patients with other forms of heart disease has been encouraging.^{12,13} Inotropic support was no longer required at the onset of labour and the cardiovascular system was stable. The peripheries were warm and pink with obvious venodilatation, which suggested that significant preloading was unlikely to be necessary.

Management of her epidural was designed to avoid hypotension and limit the total dose of local anaesthetic. Top-ups were given in the lateral position. The weaker concentration was used to minimise the maternal blood level of bupivacaine. Oxytocin has been shown to cause less disturbance in venous pressure than ergometrine¹⁴ and was therefore preferred for the third stage.

In conclusion, we find nothing from this experience to support elective Caesarean section for these patients and are pleased we resisted the pressures, although every individual will need to be assessed on her merits. Once in labour, the evidence is that an assisted vaginal delivery is the method of choice; the judicious use of lumbar epidural analgesia can facilitate this with benefit to mother and child.

Acknowledgments

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References

- KATZ H. Ueber den plotzlichen natuerlichen Tod in Schwangerschaft, Geburt und Wochenbett. *Archiv fur Gynakologie* 1921; 115: 2-83.
- GINZ B. Myocardial infarction in pregnancy. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1970; 77: 610-5.
- HUSAINI MH. Myocardial infarction during pregnancy: a report of two cases with a review of the literature. *Postgraduate Medical Journal* 1971; 47: 660-5.
- CORTIS BS, FREESE E, LUISADA AA, MOTTO S, ZUMMO B. Pre-cordial pain and myocardial infarction in pregnancy. *Giornale Italiano di Cardiologia* 1979; 9: 532-4.

5. ABBOUD TK, WILLIAMS V, HENRIKSEN EH. Anesthetic management of the parturient with a recent myocardial infarction. *Anesthesiology Review* 1980; **12**: 17-19.
6. *Report on confidential enquiries into maternal deaths in England and Wales, 1979-81*. London: Her Majesty's Stationery Office, 1983.
7. *Report on confidential enquiries into maternal deaths in England and Wales, 1976-8*. London: Her Majesty's Stationery Office, 1982.
8. *Report on confidential enquiries into maternal deaths in England and Wales, 1973-5*. London: Her Majesty's Stationery Office, 1979.
9. STOKES IM, EVANS J, STONE M. Myocardial infarction and cardiac arrest in the second trimester followed by assisted vaginal delivery under epidural analgesia at 38 weeks gestation. Case report. *British Journal of Obstetrics and Gynaecology* 1984; **91**: 197-8.
10. OSTHEIMER GW, ALPER MH. Intrapartum anesthetic management of the pregnant patient with heart disease. *Clinical Obstetrics and Gynecology* 1975; **18**: 81-97.
11. SCHNIDER SM, ABBOUD TK, ARTAL R, HENRIKSEN EH, STEFANI SJ, LEVINSON G. Maternal catecholamines decrease during labor after lumbar epidural anesthesia. *American Journal of Obstetrics and Gynecology* 1983; **147**: 13-15.
12. GOTHARD JWW. Heart disease in pregnancy. The anaesthetic management of a patient with prosthetic heart valves. *Anaesthesia* 1978; **33**: 523-6.
13. McMURRAY TJ, KENNY NT. Extradural anaesthesia in parturients with severe cardiovascular disease. Two case reports. *Anaesthesia* 1982; **37**: 442-5.
14. MOIR DD, THORBURN J. *Obstetric anaesthesia and analgesia*, 3rd edn. London: Baillière Tindall, 1980.

CASE REPORT

Injury to the axillary nerve

C. L. GWINNUTT

Summary

A case is described of a 32-year-old woman who showed signs of injury to the left axillary nerve after lumbar spine surgery. This rare complication is reviewed and the possible mechanisms of injury are discussed.

Key words

Complications; nerve injury.

Injury to the left axillary nerve in isolation is rare after anaesthesia. A case is described which occurred following surgical decompression of the lumbar spine.

Case history

A 32-year-old woman presented for elective surgical decompression of her lumbar spine. The pre-operative visit revealed that she had undergone a similar procedure in the same area 15 years previously, under general anaesthesia which she described as uneventful. The only other relevant finding was that the patient was mildly obese and weighed 80 kg. Premedication with lorazepam 2 mg and metoprolol 10 mg was given 90 minutes before operation.

Anaesthesia was induced in the supine position with thiopentone 350 mg. Neuromuscular blockade was achieved with a bolus of atracurium 50 mg and an atracurium infusion was started. The rate of the infusion was determined by the response of the adductor pollicis to train-of-four stimulation of the ulnar nerve. Anaesthesia was maintained with isoflurane in 65% nitrous oxide and oxygen, together with fentanyl 350 µg. Ventilation of the lungs was adjusted to keep the end tidal carbon dioxide concentration between 4.0 and 4.5%. The ECG was also displayed, and the systemic blood pressure monitored using a Dinamap (Critikon).

The patient was placed in a modification of the Mohammedan praying position in order to facilitate surgical access. The entire procedure lasted 150 minutes and was uneventful.

She complained of weakness and numbness in her left arm on the first postoperative day. There was marked weakness of the left deltoid muscle on examination; the patient was unable to abduct her shoulder against gravity more than 50°. There was in addition a clearly demarcated



Fig. 1. Area of decreased sensation on the patient's left arm.

area of decreased sensation over the lateral aspect of the upper arm (Fig. 1). There were no other abnormalities.

It was considered that the most likely diagnosis was injury to the left axillary nerve, as a result of the position in which the patient was placed for surgery. The patient described during the examination how she had suffered exactly the same problem after the first operation on her spine, and had made a complete recovery in the following 8 weeks. She had forgotten unfortunately to mention this at the pre-operative visit. The patient was reassured in anticipation of a full recovery, and the symptoms had resolved completely when she was seen in the outpatient department 2 months later.

Discussion

Nerve palsies following anaesthesia have been observed since before the turn of the century,¹ and in 1897 it was

suggested that nerve palsies were due to malpositioning of the patient on the operating table with consequent stretching and compression of nerves.² Many publications have described injuries to peripheral nerves as a result of lack of care in positioning patients for surgery^{3,4} but there are few reports of isolated injury to the axillary nerve. Pollock, in his review of peripheral nerve injuries, stated: 'Isolated paralysis (of the axillary nerve) is rare, but is commonly observed in brachial plexus lesions. It has been observed following prolonged stretching in sleep and anaesthesia'.⁵ Parks⁶ reviewed peripheral nerve injuries which occurred over a 13-year period and listed brachial plexus palsies as the most common injury, with the fifth and sixth motor roots of the musculocutaneous nerve as the most consistently damaged. No mention was made of the axillary nerve.

The axillary nerve arises from the posterior cord of the brachial plexus and is derived from C₅ and C₆. Initially it lies in close relation to the lowest part of the articular capsule of the shoulder joint. It then passes through a quadrangular space, lying in close proximity to the surgical neck of the humerus. It divides into two terminal branches. The anterior branch supplies the anterior part of the deltoid muscle and the overlying skin. The posterior branch supplies teres minor, the posterior fibres of deltoid and continues as the lateral cutaneous nerve of the arm. This sensory part supplies skin over the lower deltoid region and the upper part of the long head of triceps.⁷

The majority of isolated lesions of the axillary nerve arise as a result of its proximity to the head of the humerus.⁸ The nerve is stretched across the head of the humerus when the arm is abducted and externally rotated during inferior (subglenoid) dislocation. The nerve is also vulnerable to damage in patients who sustain fractures of the surgical neck of the humerus.

Damage to the axillary nerve can result in a variety of clinical manifestations. Loss of motor function and sensation can occur individually or in combination.^{2,8} It is the loss of both motor and sensory function in this case which makes axillary nerve injury the most likely diagnosis.

The nature of spinal surgery frequently necessitates that the patient is placed in abnormal positions to facilitate surgical access and to allow accurate determination of the operative level. The anaesthetised, paralysed patient is unable to protect himself from abnormal posture and so there is an increased risk of damage in this group of patients. A modification of the Mohammedan praying position⁹ was used in this case. The hips and knees are flexed to almost a right-angle and the operating table tilted 20° head up, with supports placed behind the buttocks and under the anterior chest wall. The shoulders remain extended; the arms are placed to lie above the head and rest on the operating table (Fig. 2), a position which has been described to be optimal for patients in the prone position.¹⁰ In this manner, the abdomen hangs free and weight bearing is mainly through the knees and superior iliac spines. The most likely explanation for the injury sustained by this patient is that the degree of abduction and extension at the shoulder joint in achieving this position resulted in pressure on the axillary nerve by the head of the humerus. It

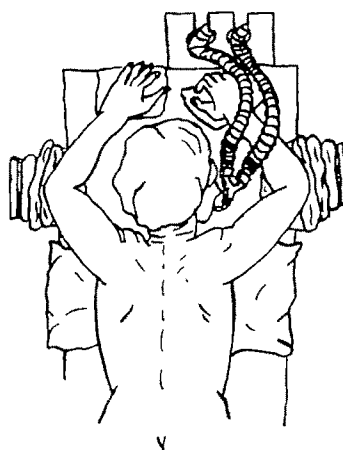


Fig. 2. Position of head, neck and arms during surgery.

is unclear why only the left side was affected on both occasions but it may represent a localised anatomical abnormality.¹¹ Further investigation of the patient was not felt to be justified because no symptoms occurred normally.

This report demonstrates that the use of recognised positions to facilitate surgical access does not automatically safeguard against injury to peripheral nerves. The problem might have been avoided if the pre-operative enquiry had elicited the information about the peri-operative events of previous surgery.

Acknowledgments

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References

1. BUDINGER K. Ueber Lahmungen nach Chloroformnarkosen. *Archiv fur Klinische Chirurgie* 1894; 47: 121-45.
2. GARRIGUES HJ. Anaesthesia—paralysis. *American Journal of Medical Science* 1897; 113: 81-9.
3. DHUNER K-G. Nerve injuries following operations: a survey of cases occurring during a 6-year period. *Anesthesiology* 1950; 11: 287-93.
4. BRITT BA, GORDON RA. Peripheral nerve injuries associated with anaesthesia. *Canadian Anaesthetists' Society Journal* 1964; 11: 514-36.
5. POLLOCK LJ, DAVIS L. Peripheral nerve injuries. *American Journal of Surgery* 1932; 17: 461-71.
6. PARKS BJ. Postoperative peripheral neuropathies. *Surgery* 1973; 74: 348-57.
7. WARWICK R, WILLIAMS PL, eds. *Gray's anatomy*, 35th edn. Edinburgh: Longmans, 1973: 1039.
8. SUNDERLAND S. *Nerve and nerve injuries*, 2nd edn. London: Churchill Livingstone, 1978.
9. DINMORE P. A new operating position for posterior spinal surgery. *Anaesthesia* 1977; 32: 377-80.
10. SMITH RH, GRAMLING ZW, VOLPITTO PP. Problems related to the prone position for surgical operations. *Anesthesiology* 1961; 22: 189-93.
11. CLAUSEN EG. Postoperative ('anesthetic') paralysis of the brachial plexus; review of the literature and report of 9 cases. *Surgery* 1942; 12: 933-42.

CASE REPORT

Anaphylactoid reaction to vecuronium followed by systemic reaction to skin testing

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Summary

An unusual case is presented of a systemic anaphylactoid reaction to tubocurarine and subsequently to vecuronium. Intradermal testing with vecuronium following the latter response was negative at recommended test dose levels but at a higher concentration it initiated a hazardous systemic response. The laboratory investigations and possible mechanisms involved in this unusual case are discussed in detail since they may relate to other patients who experience anaphylactoid responses to anaesthetic drugs and who then undergo intradermal testing.

Key words

Complications; skin testing, systemic anaphylactoid reactions. Neuromuscular blocking drugs; vecuronium.

Modern balanced anaesthesia involves the intravenous administration of several potent drugs which possess different pharmacological activities. These drugs are administered in close proximity to each other so it is hardly surprising that interactions and untoward immediate (anaphylactoid) responses occur. The latter frequently implicate the chemically highly reactive neuromuscular blocking drugs.

Vecuronium has been reported to produce generalised erythema,¹ hypotension² and bronchospasm.^{3,4} The present case illustrates a severe reaction to vecuronium in a patient with a previous history of anaphylactoid reaction to tubocurarine. The paper presents the results of immunological investigations on blood samples taken during and after the reaction, and of intradermal testing which led to a further systemic anaphylactoid reaction.

Case history

A 42-year-old woman presented for cervical microdiscectomy. She had a long history of hayfever and asthma that required daily salbutamol and beclomethasone inhalers; however, there was no wheezing on pre-operative examination.

Uneventful anaesthesia for tubal ligation in 1979 had involved the use of papaveretum, hyoscine, thiopentone, fentanyl, alcuronium and ventilation with nitrous oxide and oxygen. Muscle relaxation was antagonised after surgery using atropine and neostigmine and there were no postoperative problems. Thiopentone, tubocurarine and

fentanyl were given on the occasion of her next anaesthetic for hysterectomy in 1980, prior to tracheal intubation and ventilation of the lungs with nitrous oxide, oxygen and 0.5% halothane. She developed an airway pressure greater than 5 kPa 10 minutes after induction of anaesthesia, and the ventilator failed to cycle. There was no bronchospasm, muscle rigidity, pyrexia or tracheal tube problem. She then became flushed and hypotensive, and an anaphylactoid reaction was presumed. Aminophylline, chlorpheniramine and hydrocortisone produced only a slight improvement in ease of ventilation. Two litres of crystalloid were given to achieve a systolic arterial pressure greater than 100 mmHg. Peri-orbital oedema and slight laryngeal oedema were then noted. Tubocurarine was the only agent which she had not received previously and it was to this drug that the reaction was attributed.

It was decided that histamine-releasing drugs should be avoided during her most recent anaesthetic. She was pre-medicated with diazepam 15 mg and had used her salbutamol and beclomethasone inhalers as normal. Chlorpheniramine 10 mg was given prior to induction of anaesthesia with etomidate 15 mg, vecuronium 6 mg and fentanyl 0.2 mg; further doses of vecuronium 2 mg and fentanyl 0.1 mg were given. Her trachea was intubated easily with a cuffed red rubber Oxford tube (with a Murphy's eye) and her throat packed with damp gauze. Anaesthesia was maintained with nitrous oxide, oxygen and 0.5% halothane. Vecuronium was infused at 2–3 mg/hour. Surgery at this time involved local infiltration of 20 ml lignocaine 1% with

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adrenaline 1:200 000 into the operative site. The inflation pressure increased to 6 kPa as the patient's head was turned during radiography 50 minutes after induction of anaesthesia, and the end tidal CO₂ concentration decreased. Manual ventilation with 100% oxygen was started. On auscultation, air entry to both sides was minimal and so no wheezing was heard. The possibilities that the tracheal tube had kinked or become misplaced, or that the cuff had herniated were excluded (a suction catheter was passed easily) and the patient began to cough. A bolus dose of vecuronium 2 mg was given. The systolic arterial pressure decreased to less than 60 mmHg and she became flushed, sweaty and impossible to ventilate. The administration of adrenaline 100 µg intravenously and adrenaline 100 µg via the tracheal tube was followed by an immediate improvement in the ease of ventilation, and some wheezing could then be heard. Hydrocortisone 100 mg and one litre of human albumin were given, and the systolic arterial pressure gradually increased to 110 mmHg. Blood samples were taken into EDTA (ethylenediamine tetra-acetic acid) and plain bottles for complement and immunoglobulin assays, and despatched immediately to the Protein Reference Laboratory at Sheffield.

It has been suggested that red rubber tracheal tubes may be allergenic⁵ and so hers was replaced by a plastic tube. Slight vocal cord oedema, facial swelling and an erythematous rash on the legs and trunk were noted. Surgery was abandoned and she was transferred to the intensive care unit where she recovered completely following administration of further intravenous fluid.

Further blood samples were taken into EDTA at 3, 6 and 24 hours for complement and immunoglobulin assays and automated full blood count profile. The blood for complement and immunoglobulin assays was centrifuged and the plasma separated and stored at -20°C until despatched to the Protein Reference Laboratory at Sheffield. Skin tests were performed 22 weeks later.

Results

The results of the haematological, immunoglobulin and complement assays are shown in Table 1. The cellular changes may be attributable to the bolus of hydrocortisone given. Most of the other changes illustrate some degree of haemodilution; the immunoglobulins decreased at 3 and 6 hours but returned by 24 hours to levels the same as, or higher than those seen at the time of the reaction. These results are all within the normal ranges except for the

plasma IgE levels which are well above the median population level of 25 IU/ml and show proportionally more marked movement than is seen with any of the other proteins. The changes of complement protein parallel those of the immunoglobulins and are all within normal ranges.

Prick tests to etomidate, alcuronium, pancuronium and vecuronium together with saline and histamine controls revealed no positive allergic responses. Intradermal testing⁶ with 0.1 ml of a 1:100 dilution of working-strength etomidate and 0.1 ml of 1:1000 dilutions of working-strength alcuronium, pancuronium and vecuronium, equivalent to absolute doses of 0.2, 0.5, 0.2 and 0.2 µg, respectively, also revealed no allergic responses. However, the patient did complain of local discomfort on injection of 5 µg of the histamine control, which caused erythema and a wheal of 15 mm at 10 minutes.

Positive skin tests have been reported previously after intradermal testing of a 1:10 dilution of working-strength vecuronium.⁴ Consequently, it was decided, with the patient's informed consent, to test intradermally with 0.1 ml of a 1:100 dilution of working-strength vecuronium (equivalent to 2 µg). The patient complained of a local stinging sensation after the injection and, within 2 minutes, of 'light-headedness' and tightness in the chest. Her respiratory rate increased from 12 to 17 breaths/minute and systolic arterial pressure decreased from 140 to 135 mmHg; heart rate increased from 95 to 105 beats/minute. Auscultation of the chest revealed slight expiratory wheeze in all areas. Intravenous injection of ranitidine 50 mg and chlorpheniramine 25 mg produced temporary relief of bronchospasm. The skin test was positive 10 minutes after the injection, with a 10 mm wheal, and the bronchospasm returned. She was given aminophylline 200 mg and hydrocortisone 100 mg intravenously. Her symptoms subsided gradually over the next hour; the skin test was still positive after 30 minutes. She had no bronchospasm 4 hours later.

Discussion

The patient presented a puzzling array of apparent parallels mixed with contradictions. Her first recorded adverse response, to tubocurarine in 1980, appeared to be a direct histamine release response rather than a drug-specific antibody-mediated reaction. On this basis, histamine-releasing drugs were avoided during her most recent anaesthetic.

The induction of anaesthesia with fentanyl, etomidate and vecuronium was uneventful. She received two further doses of vecuronium without apparent problem and de-

Table 1. Haematological, immunoglobulin and complement investigations at the time of, and following anaphylactoid reaction to vecuronium.

Time	Haematological indices			Immunological assays				RAST¶ (grade) to		Complement assays		
	Total leucocytes (× 10 ⁹ /litre)	Neutrophil/leucocyte ratio	Haematocrit	IgG (g/litre)	IgA (g/litre)	IgM (g/litre)	IgE (IU/ml)	TGP*	HDM†	C ₃ (g/litre)	C ₄ (g/litre)	C _h Inh. (g/litre)
At time of reaction‡	7.2	0.6	0.41	8.1	1.8	0.7	181	2	0	0.64	0.22	0.16
3 hours	n.d.§	n.d.	n.d.	6.9	1.5	0.5	118	n.d.	n.d.	0.55	0.20	n.d.
6 hours	16.4	0.9	0.32	6.8	1.5	0.4	137	n.d.	n.d.	0.60	0.19	n.d.
24 hours	12.4	0.8	0.32	8.3	1.9	0.6	182	n.d.	n.d.	0.77	0.26	n.d.

¶ Radio allergic sorbent test.

* Timothy grass pollen.

† House dust mite.

‡ Haematological indices derived from 2-day pre-operative specimen.

§ Not done.

veloped a fully systemic anaphylactoid response only upon the addition of a further bolus of vecuronium. It would be hard to inculcate antibodies, whatever the mechanism. It would not be hard to inculcate binding onto different specific receptor sites on various sensitive cells. This may explain the IgE fluctuation which could reflect mast cell repopulation after non-immune activation, although it is usually associated with antibody-mediated reactions. The quaternary ammonium moiety is the common binding group in all neuromuscular drugs so the similar behaviour by curare and vecuronium can be explained to some extent.

Since the reaction was circumstantially triggered by vecuronium, whether by immune or non-immune mechanisms, skin testing was performed. There was no reaction to either prick testing or the intradermal test at the initial dilutions. It would have been justified at this point to report that the patient was not sensitive to vecuronium. However, on the basis of previous experience with vecuronium, and with the patient's consent, the intradermal test concentration was increased ten-fold and this produced the marked systemic anaphylactoid response. The parallel with her previous clinical adverse experience is clear but the mechanism is less certain.

It seems unlikely that antibodies were involved at all. The response was more in keeping with a dose-dependent direct histamine release reaction, and speculative explanations may be made for the reactions as follows.

There is evidence in anaphylactoid reactions to anaesthetic agents that whilst pretreatment with steroids or antihistamine alone may not be protective,⁷ together they may be.⁸ Pretreatment with H₁ and H₂ blockers⁹ or with H₁ blockers and steroids has been advocated¹⁰ together with the possible addition of subcutaneous adrenaline. In the present case, the patient had used her salbutamol and beclomethasone inhalers as normal pre-operatively, and she was given chlorpheniramine 10 mg immediately before induction of anaesthesia with fentanyl, etomidate and vecuronium. This may have gone some way to reduce plasma histamine release, block the effects of released histamine, or both. The operative site was infiltrated locally with 20 ml lignocaine 1% with adrenaline 1:200 000 as part of the surgical procedure; this is equivalent to 1 ml adrenaline 1:10 000 and may also have contributed to the delay in onset of the clinically apparent reaction.

The anaphylactoid reaction appeared before the final bolus of vecuronium, which may have exacerbated the reaction from one of respiratory involvement only to a full systemic response and possibly illustrates the suggested dose-dependent reaction.

The negative reaction to 0.2 µg in the intradermal tests, but local and systemic responses to 2.0 µg may be a further expression of a dose-related reaction. Alternatively, the first dilution used may have acted in a locally permissive way to allow a greater, and subsequently systemic, reaction to the second dilution.

The patient's response to the histamine control was cer-

tainly avid but was without systemic accompaniment. However, this probably reflects more of a difference between generation and release of histamine and other mediators *in situ*, and exogenous administration of histamine. Perhaps the patient's response is typical of one with mastocytosis, a condition which is stimulated particularly by intravenous therapy and is certainly more common than previously recognised.

Any other explanation of this highly complex series of events would be welcomed. Whatever the mechanism, a dangerous reaction which required aggressive treatment was produced during intradermal testing of this patient. The emergency situation was generated in a location and with personnel equipped and experienced to deal with the adverse reaction. This surely justifies previous warnings that such testing should be carried out not at random by clinicians but in centres able to perform these studies with full recovery facilities available immediately. The reaction was undoubtedly due to vecuronium and not to a needle reaction since bronchospasm returned as the effects of the H₁ and H₂ antagonists wore off some 10 minutes later.

This case emphasises the fact that initial conclusions drawn from skin testing may be erroneous. This may also apply to one or more of the other drugs tested only at the initial dilution in this patient. Finally, what can we tell the patient, and what neuromuscular blocking drugs can she be given safely in the future? The potential legal implications are obvious.

References

1. CLAYTON DG, WATKINS J. Histamine release with vecuronium. *Anaesthesia* 1984; **39**: 1143-4.
2. LAVERY GG, HEWITT AJ, KENNY NT. Possible histamine release after vecuronium. *Anaesthesia* 1985; **40**: 389-90.
3. CONIL C, BORNET JL, JEAN-NOEL M, CONIL JM, BROUCHET A. Choc anaphylactique au pancuronium et au vecuronium. (Anaphylactic shock caused by pancuronium and vecuronium.) *Annales Francaises d'Anesthesie et de Reanimation* 1985; **4**: 241-3.
4. O'CALLAGHAN AC, SCADDING G, WATKINS J. Bronchospasm following the use of vecuronium. *Anaesthesia* 1986; **41**: 940-2.
5. BASAVARAJA HM, FIRN S, WATKINS J. A possible case of red rubber sensitivity. *Anaesthesia* 1986; **41**: 549-50.
6. FISHER MMCD. Intradermal testing in the diagnosis of acute anaphylaxis during anaesthesia—results of five years' experience. *Anaesthesia and Intensive Care* 1979; **7**: 58-61.
7. FISHER MMCD, MORE DG. The epidemiology and clinical features of anaphylactic reactions in anaesthesia. *Anaesthesia and Intensive Care* 1981; **9**: 226-34.
8. LORENZ W, DOENICKE A, MEYER R, REIMANN HJ, KUSCHE J, BARTH H, GEESING H, HUTZEL M, WEISSENBACHER B. Histamine release in man by propanidid and thiopentone: pharmacological effects and clinical consequences. *British Journal of Anaesthesia* 1972; **44**: 355-69.
9. WATKINS J, WILD G, CLARKE RSJ. Allergy, plasma IgE level and anaphylactoid response: a hypothesis. *Anaesthesia* 1985; **40**: 362-5.
10. FISHER MMCD. The prevention of second anaphylactoid reactions to anaesthetic drugs. *Anaesthesia and Intensive Care* 1981; **9**: 242-6.

CASE REPORT

Epidural fentanyl and monoamine oxidase inhibitors

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Summary

The successful use of continuous epidural fentanyl infusion to control postoperative pain in a patient treated with monoamine oxidase inhibitors is described. The use of epidural opioids may be a safe technique for the management of such patients.

Key words

Anaesthetic techniques, regional; epidural.

Analgesics, narcotic; fentanyl.

Adverse reactions following the use of narcotic analgesic drugs in patients treated with monoamine oxidase inhibitors (MAOIs) are well recognised. Respiratory depression, hyperpyrexia, convulsions, coma and death have all been reported to follow the use of narcotics, especially pethidine.^{1–4} However, systemic analgesics (opioids and non-opioids) and local anaesthetic techniques have been used to provide pain relief. It is important to avoid sympathetic overactivity in this group of patients, who are prone to hypertensive crises. Spinal opioids have been shown to be a superior technique compared with the conventional methods in the provision of analgesia and better pulmonary function.⁵ We describe here the use of epidural fentanyl in a patient who received monoamine oxidase inhibitors (MAOIs). This has not been reported before in the literature.

Case history

A 71-year-old female patient, weight 50.8 kg, presented for abdominoperineal excision of the rectum for adenocarcinoma. For 12 years she had been taking tranylcypromine and trifluoperazine (Parstelin) for depression. Her other significant past medical history included tuberculosis, hypertension controlled with amiloride (Moduretic) and mild asthma which was treated with salbutamol and beta-methasone inhalers. Examination revealed an anxious woman with a regular heart rate of 76 beats/minute and arterial blood pressure of 130/70 mmHg. The only abnormal physical sign was mild expiratory wheeze, and laboratory investigations were within the normal range.

A decision was taken in conjunction with the psychiatrist not to stop MAOIs. Premedication was with temazepam 10 mg orally and all her normal drugs but she was still

anxious on arrival in the anaesthetic room. A test dose of fentanyl 20 µg and diazepam (Diazemuls) 2 mg was given intravenously. The left radial artery was cannulated and a central venous pressure (CVP) catheter inserted via a right antecubital vein under local anaesthesia. Arterial blood pressure, pulse rate, ECG and general state of awareness were unchanged after 25 minutes. Another dose of fentanyl 20 µg and diazepam 2 mg was administered intravenously with no sequelae. An epidural catheter was inserted into the L_{1/2} interspace and advanced 3 cm cephalad. Induction of anaesthesia and tracheal intubation were carried out with etomidate 20 mg and alcuronium 20 mg. Anaesthesia was maintained with nitrous oxide 70% and isoflurane 0.5–1% in oxygen.

Five millilitres bupivacaine 0.25% plain were administered through the epidural catheter 10 minutes before the surgical incision, and the same dose repeated 1.5 hours after the start of surgery. The estimated blood loss was 3200 ml and the urine output totalled 380 ml. Circulating volume was maintained with 7 units packed red cells, 3 units human plasma protein fraction, 2 units fresh frozen plasma and 1000 ml Hartmann's solution.

A bolus of fentanyl 50 µg (concentration 10 µg/ml) was administered epidurally 15 minutes before the end of the surgical procedure, and a continuous epidural infusion of fentanyl started at a rate of 60 µg/hour in the same concentration as the bolus dose.

The operation lasted 2.5 hours, after which muscle relaxation was reversed with glycopyrronium 0.6 mg and neostigmine 2.5 mg. The patient awakened promptly and was moved, conscious and pain free, to the recovery room where she breathed 40% oxygen in air from an Accurox facemask. Arterial blood pressure and CVP were monitored

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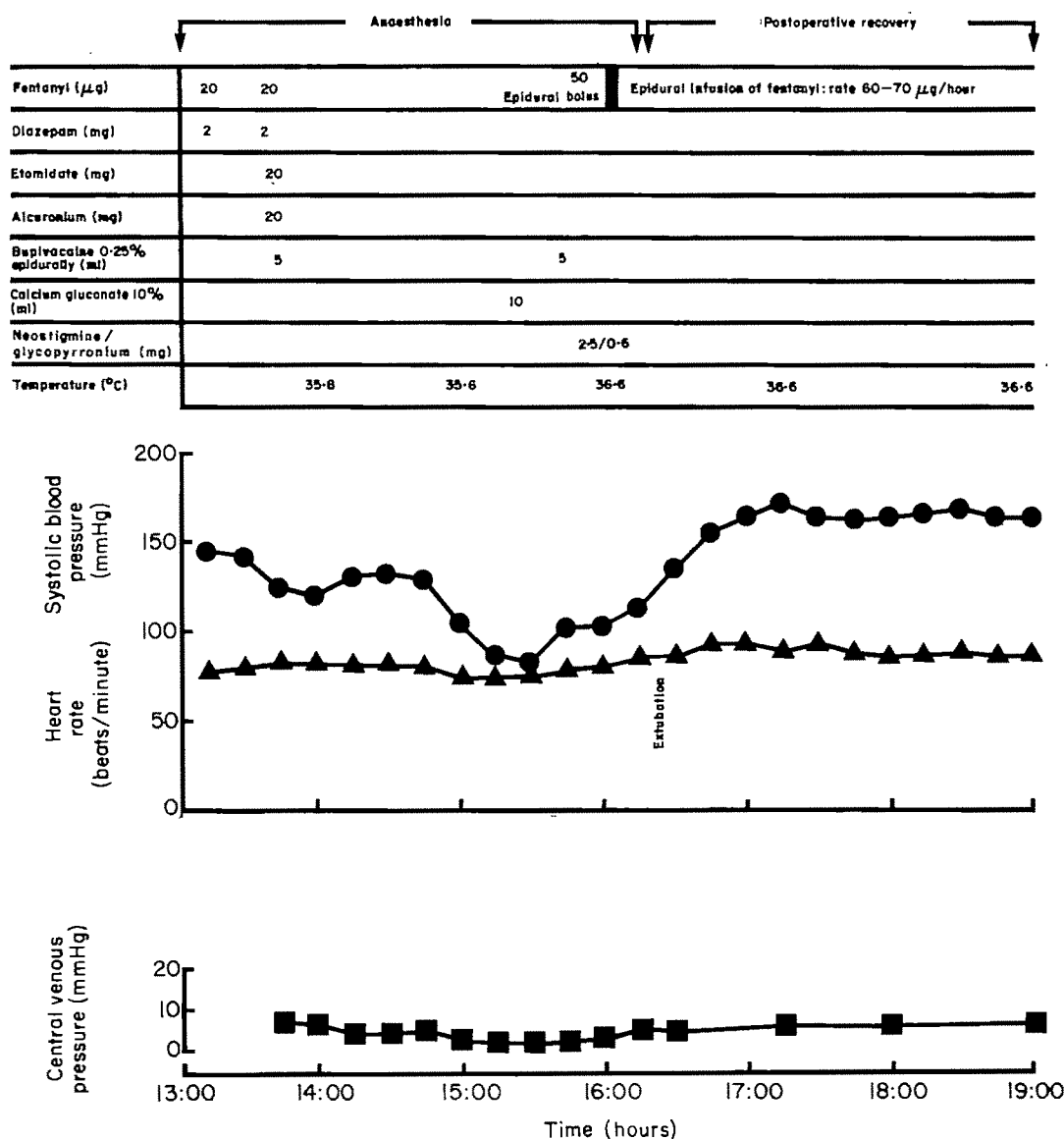


Fig. 1. Physiological measurements and administration of drugs during surgery and in the immediate postoperative recovery period. ●—●, Systolic blood pressure; ▲—▲, heart rate; ■—■, central venous pressure.

directly and continuously. Respiratory rate and temperature were recorded half-hourly for 2 hours in the recovery room. Figure 1 summarises the anaesthetic sequence.

The patient returned to the general surgical ward after 2 uneventful hours in the recovery room. In addition to routine observations, nursing staff were specially instructed to measure pulse rate and respiratory rate half-hourly for as long as the epidural fentanyl infusion was in progress. They were warned to stop the epidural infusion and inform the anaesthetist on call immediately if the patient's respiratory rate decreased below 10 breaths/minute.

The epidural infusion was continued for 4 days, at a rate of 50–70 μ g/hour. The patient was allowed to take her own MAOI tablets on the third postoperative day and subsequent progress was uneventful.

Discussion

MAOIs exert their antidepressant effect by inhibition of the degradation of various amines, including serotonin, dopa-

mine and noradrenaline.⁶ They lead to accumulation of noradrenaline at the peripheral nerve endings. The oxidative liver enzymes are also inhibited. The first adverse reaction following the use of an analgesic drug in a patient treated with MAOIs, was reported in 1955¹ and numerous cases have since been published. The opioid was pethidine in every case but one.⁷ The mechanisms by which pethidine and MAOIs interact are not well understood.^{8,9} Pethidine has been shown to cause hyperpyrexia, convulsion and death in some animal models and this was found to be related to the inhibition of serotonin re-uptake in the central nervous system.¹⁰

However, many patients who receive these antidepressants have reacted quite normally when given opioids.¹¹ An opioid sensitivity test has been recommended before their use in such patients.^{11,12} Chlorpromazine² and prednisolone³ should be administered in case of an adverse reaction, and other supportive measures should also be started immediately to combat respiratory depression and hyperpyrexia. The anaesthetic management of patients who

receive MAOIs can be a difficult task and analgesia is a real problem. Several approaches and techniques have been suggested but none is without risk.

Local anaesthesia may be used but this is not always feasible and care should be exercised in calculating the maximum safe dose of local anaesthetic for any particular technique because of inhibition of liver enzymes by MAOIs. If a regional technique (spinal or epidural) is to be used, then the accompanying hypotension is problematical and even dangerous to treat. Indirect sympathomimetics, for example ephedrine, are contraindicated because they can lead to excessive release of the accumulated noradrenaline at the sympathetic nerve endings.¹³ Volume loading should be the first line of treatment in such events; noradrenaline infusion has been used successfully in the past.¹⁴

Alternatively, should general anaesthesia be the technique of choice, the operation should be postponed for 2 weeks while the drug is discontinued.¹⁵ This may carry the risk of relapse of depression and is not applicable in emergency situations.

Adequate postoperative pain relief in such patients should be planned carefully to avoid autonomic hyperactivity. Many techniques of spinal and epidural opioid administration have been developed since the discovery of opioid receptors in the spinal cord. Epidural fentanyl has been shown to provide better analgesia and respiratory function compared with conventional intramuscular papaveretum.⁵ Fentanyl is highly lipophilic compared with other opioids (e.g. morphine) and it should hence give segmental analgesia when it is given epidurally, with less chance of rostral spread in the cerebrospinal fluid and subsequent late respiratory depression.¹⁶ Also, plasma concentrations of fentanyl following epidural use are reported to be well below those generally associated with systemic effect.^{5,17} This latter pharmacokinetic characteristic of fentanyl is particularly desirable in order to avoid drug interaction with MAOIs.

Fentanyl does not cause histamine release¹⁸ and it has also been found to have an antihistaminic effect.¹⁹ Consequently, it was thought that fentanyl might be an ideal drug to use in our case to avoid the problems of hypotension due to histamine release and to guard against bronchospasm in an asthmatic patient. It has been shown in animals that fentanyl has an antiserotonergic action.¹⁹ This could, in theory, protect patients who receive MAOIs from the central side effects of opioids, as discussed previously in relation to pethidine.

In conclusion, adequate pain relief in patients who receive MAOIs is vital. Epidural fentanyl is suggested to be a safe technique in patients who receive MAOIs.

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References

1. MITCHELL RS. Fatal toxic encephalitis occurring during iproniazid therapy in pulmonary tuberculosis. *Annals of Internal Medicine* 1955; **42**: 417-24.
2. PAPP C, BENAÏM S. Toxic effects of iproniazid in a patient with angina. *British Medical Journal* 1958; **2**: 1070-2.
3. SHEE JC. Dangerous potentiation of pethidine by iproniazid, and its treatment. *British Medical Journal* 1960; **2**: 507-9.
4. TAYLOR DC. Alarming reaction to pethidine in patients on phenelzine. *Lancet* 1962; **2**: 401-2.
5. WELCHEW EA, THORNTON JA. Continuous thoracic epidural fentanyl. A comparison of epidural fentanyl with intramuscular papaveretum for postoperative pain. *Anaesthesia* 1982; **37**: 309-16.
6. BALDESSARINI RJ. Drugs and the treatment of psychiatric disorders. In: GILMAN AG, GOODMAN LS, GILMAN A, eds. *The pharmacological basis of therapeutics*. New York: Macmillan, 1980: 427-30.
7. SPENCER GT, SMITH SE. Dangers of monoamine oxidase inhibitors. *British Medical Journal* 1963; **1**: 750.
8. FULLER RW, SNOODY HD. Inhibition of serotonin uptake and the toxic interaction between meperidine and monoamine oxidase inhibitors. *Toxicology and Applied Pharmacology* 1975; **32**: 129-34.
9. JOUNELA AJ, MATTILA MJ, KNOLL J. Interaction of selective inhibitors of monoamine oxidase with pethidine in rabbits. *Biochemical Pharmacology* 1977; **26**: 806-8.
10. SINCLAIR JG, LO GF. The blockade of serotonin uptake and the meperidine-monoamine oxidase inhibitor interaction. *Proceedings of the Western Pharmacology Society* 1977; **20**: 373-4.
11. EVANS-PROSSER CDG. The use of pethidine and morphine in the presence of monoamine oxidase inhibitors. *British Journal of Anaesthesia* 1968; **40**: 279-82.
12. CHURCHILL-DAVIDSON HC. Anaesthesia and monoamine oxidase inhibitors. *British Medical Journal* 1965; **1**: 520.
13. PERKS ER. Monoamine-oxidase inhibitors. *Anaesthesia* 1964; **19**: 376-86.
14. PELLIS COCKS D, PASSMORE-ROWE A. Dangers of monoamine oxidase inhibitors. *British Medical Journal* 1962; **2**: 1545-6.
15. ROIZEN MF. Preoperative evaluation of patients with diseases that require special preoperative evaluation and intraoperative management. In: MILLER RD, ed. *Anesthesia*. New York: Churchill Livingstone, 1981: 21-93.
16. BROMAGE PR, CAMPORESI EM, DURANT PAC, NEILSEN CH. Rostral spread of epidural morphine. *Anesthesiology* 1982; **56**: 431-6.
17. WOLFE MJ, DAVIES GK. Analgesic action of extradural fentanyl. *British Journal of Anaesthesia* 1980; **52**: 357-8.
18. ROSOW CE, MOSS J, PHILBIN DM, SAVARESE JJ. Histamine release during morphine and fentanyl anesthesia. *Anesthesiology* 1982; **56**: 93-6.
19. TODA N, HATANO Y. Contractile responses of canine tracheal muscle during exposure to fentanyl and morphine. *Anesthesiology* 1980; **53**: 93-100.

CASE REPORT

Fatal paradoxical thrombo-embolism during anaesthesia

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Summary

Deep venous thrombosis is a recognised complication of trauma to the leg and may lead to pulmonary thrombo-embolism, but paradoxical thrombo-embolism is rare. A case of fatal paradoxical thrombo-embolism which followed a leg injury in a previously fit 36-year-old male is presented and contributory factors are reviewed.

Key words

Embolism; thrombo-embolus, paradoxical.

Case history

A healthy male aged 36 years sustained a major ligamentous injury and dislocation of his left knee while playing rugby. The dislocation was reduced under general anaesthesia and immobilised in a long leg plaster cast at another hospital. The patient underwent surgical repair of the torn ligaments 36 hours later. Thiopentone 500 mg, papaveretum 20 mg and atracurium 40 mg were administered intravenously, the trachea was intubated and anaesthesia was maintained with enflurane and nitrous oxide in 33% oxygen, delivered by intermittent positive pressure ventilation. Twenty millilitres of 0.5% plain bupivacaine were injected around the left femoral nerve below the inguinal ligament. A tourniquet was applied to the left thigh and inflated to 300 mmHg for 100 minutes without Esmarch compression. The repair of the ligaments was uneventful and the electrocardiograph (ECG) was stable throughout the 3-hour procedure. Systolic arterial blood pressure, measured by oscillotonometer, remained between 110 and 130 mmHg apart from a transient decrease to 90 mmHg immediately after release of the tourniquet. Spontaneous respiration recommenced shortly after administration of the anaesthetic gases was discontinued and the patient's trachea was then extubated.

It became apparent after one hour in the recovery room, during which time he remained very drowsy, that he had a dense right hemiplegia and total aphasia. Blood coagulation studies, haematology and biochemistry at this time were normal. Arterial blood gas analysis revealed mild hypoxaemia (arterial oxygen tension 8.7 kPa) while the patient breathed room air.

The patient's level of consciousness deteriorated. A computerised axial tomographic brain scan 8 hours post-operatively revealed complete occlusion of the distal portion of the left internal carotid artery and infarction of the left cerebral hemisphere. Signs of brainstem death were present 24 hours later despite appropriate supportive treatment and the heart, kidneys, adrenals and pancreas were removed for transplantation.

There was a large bruise in the left vastus medialis muscle at autopsy, with mural thrombus for a length of 10 cm in the adjacent femoral vein, which was judged by the pathologist to be related to the original blow to the thigh. There was no sign of venous damage at the level of the femoral nerve block. The profunda femoris vein and the more distal vessels were all patent. There were several moderate-sized pulmonary clot emboli in both lungs, and the distal left internal carotid artery had been occluded by clot embolus. The transplant team reported that the donor heart, now functioning satisfactorily in the recipient, had been noted at the time of transplantation to have a probe patent foramen ovale (PFO).

Discussion

Occlusion of the patient's left internal carotid artery could have arisen in one of three ways. The first is by embolism from the left side of the heart. Such an event is rare in the absence of mitral stenosis, atrial fibrillation or myocardial infarction,¹ and our patient had no sign of any predisposing condition. The ECG was normal throughout and the car-

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diovascular system remained stable. Postoperative clinical circumstances precluded echocardiography² to visualise the left heart anatomy and movement.

Secondly, carotid artery occlusion could have occurred from thrombosis arising *in situ*. Arterial thrombosis is rare in the absence of vessel wall damage,³ probably because of the normally rapid flow of blood through the arterial system. There was no trauma to the neck at the time of the initial injury or during subsequent surgery. The head was maintained in the midline position throughout anaesthesia and the tapes that secured the tracheal tube were tied without undue tension. There was no marking of the skin of the neck postoperatively and both common carotid pulses were noted to be present and equal. Significant pre-existing narrowing of the carotid artery, such as congenital stenosis, could not be excluded at the time of diagnosis of cerebral infarction but there were no features in the past medical history to suggest it.

Thirdly, carotid occlusion could have occurred as a result of paradoxical embolism, defined as the transmission of material from the venous circulation into arteries through a right-to-left shunt. The requisites for such a diagnosis are: a source of embolus; an intracardiac defect or pulmonary arterio-venous malformation which permits flow from the right to the left sides of the circulation; and an arterial embolus arising from a site other than the left side of the heart.

We recognised, in retrospect, that there was a high probability of deep venous thrombosis (DVT) in the injured limb. Trauma, surgery and immobilisation are prominent risk factors.⁴⁻⁶ Venous stasis, whether due to bed rest or to the presence of a plaster cast, combined with another risk factor such as trauma, greatly increases the likelihood of thrombosis,⁷ as does injury to the lower limb.

Knee dislocation is an uncommon injury and implies that a substantial disruptive force has been applied to the joint. Associated vascular damage is common. O'Donnell *et al.*⁸ reported a 30% incidence of venous injury after knee dislocation and recommended consideration of postoperative anticoagulation or prophylactic subcutaneous heparin. Theirs might be considered a conservative estimate of the frequency of venous thrombosis in view of a quoted incidence of 80% following *elective* knee surgery.⁷

Our patient had no symptoms of DVT pre-operatively and there were no signs of DVT on clinical examination out of plaster. However, prompt diagnosis of DVT frequently requires a high index of suspicion, since clinical symptoms and signs are absent in over 50% of cases.⁹

There were no physical, radiological or electrocardiographic signs of a permanent right-to-left shunt. The presence of a PFO, which would permit *temporary* shunting during periods of elevated right heart pressures, was not suspected by us prior to death. However, Leonard *et al.*¹⁰ found PFO to be the most commonly associated cardiac lesion in a series of 25 cases of paradoxical embolism diagnosed during life. Thompson and Evans¹¹ reported a combination of PFO and pulmonary embolism in over 50% of cases of paradoxical embolism. They found the incidence of 'pencil patent' PFO (0.7–1 cm diameter) in a series of 1000 unselected autopsies, to be 6% and that of 'probe patent' PFO (0.2–0.6 cm diameter) 29%.

Elevation of right heart pressure is a necessary precondition for paradoxical embolism. Such elevation is unlikely to have been long-standing in our patient, a previously fit

man, but various factors may have contributed to an acute increase peri-operatively. The occurrence of pulmonary embolism (PE) may cause right heart pressures to increase by virtue of a mechanical occlusion of the vascular tree and a release of vasospastic factors into the pulmonary circulation. PE was the most common cause of acutely elevated right heart pressures in Leonard's series.¹⁰ Intermittent positive pressure ventilation may produce an increase in pulmonary arterial pressure¹² and hence in right heart pressures. Nitrous oxide has been shown to increase pulmonary vascular resistance in certain subjects,¹³ and was administered to this patient. Deflation of the thigh tourniquet and reperfusion of the leg after an ischaemic period of 100 minutes is likely to release blood with low oxygen tension, increased potassium and metabolites and low pH to the right side of the heart. Pulmonary venous oxygen tension influences pulmonary vascular resistance according to the inspired oxygen concentration.¹⁴ There is an increase in pulmonary vascular resistance when pulmonary venous oxygen tension decreases in isolated lungs ventilated with 21% or 30% oxygen (as in our patient). Acidosis, and perhaps, increased potassium ion concentration, may also contribute to such an increase.

Deflation of the tourniquet probably dislodged clot emboli from the leg to the pulmonary bed and was followed by a transient decrease in systemic arterial pressure. We suggest, therefore, that this was the most likely time for reversal of pressure gradient and transmission of clot embolus through the PFO.

Higgins *et al.*² demonstrated the transient nature of the shunt in a patient with paradoxical thrombo-embolism via a PFO. Contrast echocardiography during the acute stages of pulmonary and systemic embolism showed right-to-left flow but, when repeated at a later date, shunting was demonstrated only during a Valsalva manoeuvre. We did not recognise the possibility of intermittent shunting and the diagnosis was not made antemortem since the patient had no postoperative signs of elevated right heart pressures or right-to-left flow. Successful diagnosis thus requires an awareness that a PFO may exist in a previously healthy patient, recognition of a source of embolus and a search for evidence of pulmonary embolism. The shunt may be transient, so contrast echocardiography may subsequently be normal.

Leonard *et al.*¹⁰ recommend immediate anticoagulation when a diagnosis of paradoxical thrombo-embolism is made, to prevent further pulmonary or paradoxical embolisation. Local surgery may be indicated for accessible systemic emboli, or thrombolytic therapy when the site is non-cerebral. Long-term anticoagulation is advisable unless a well-defined and short-lasting predisposing factor underlies the initial embolic episode. Late closure of the right-to-left communication, or inferior vena caval interruption, should be considered in the long-term management of patients with a large intracardiac defect and permanent shunting.

Prophylaxis of paradoxical thrombo-embolism requires prevention of DVT and the avoidance of elevated right heart pressures. The two are, to some extent, related since PE is an important factor in the promotion of such elevated pressures.

The high risk of DVT after a severe knee injury has already been mentioned. The role of DVT prophylaxis in patients who undergo hip or knee surgery was recently

reviewed by Hull and Raskob,¹⁵ who recommended the use of warfarin, adjusted dose subcutaneous heparin or intermittent pneumatic limb compression in combination with dextran infusion for patients who undergo elective hip or knee surgery or emergency hip surgery. Unfortunately, neither the incidence of thrombo-embolic complications after emergency knee surgery nor the appropriate form of prophylaxis has been identified, but the high risks of DVT after elective knee surgery, and of vascular damage during knee dislocation, lead us to believe that the incidence is likely to be significant and that preventive measures are warranted.

Such measures adopted at the time of the original joint reduction in our patient might have prevented DVT but would probably have caused substantial bleeding into the joint. Prophylaxis at the time of the second operation would have been too late, since thrombo-embolism had already occurred. It appears that the optimal course is to perform the definitive joint repair as soon as possible after injury and then to institute warfarin or dextran therapy post-operatively.

References

1. EDWARDS EA, TILNEY N, LINDQUIST RR. Causes of peripheral embolism and their significance. *Journal of the American Medical Association* 1966; **196**: 133-8.
2. HIGGINS JR, STRUNK BL, SCHILLER NB. Diagnosis of paradoxical embolism with contrast echocardiography. *American Heart Journal* 1984; **107**: 375-7.
3. ANDERSON JR, ed. *Muir's textbook of pathology*, Vol. 10, 12th edn. London: Edward Arnold, 1985: 14.
4. NICOLAIDES AN, IRVING D. In: NICOLAIDES AN, ed. *Thrombo-embolism. Aetiology, advances in prevention and management*. Lancaster, England: Medical and Technical Publishing Co., Ltd, 1975: 193-204.
5. MORRIS GK, MITCHELL JRA. The aetiology of acute pulmonary embolism and the identification of high risk groups. *British Journal of Hospital Medicine* 1977; **18**: 6-12.
6. SEVITT S, GALLAGHER N. Venous thrombosis and pulmonary embolism. A clinico-pathological study in injured and burned patients. *British Journal of Surgery* 1961; **48**: 475-89.
7. MCKENNA R, BACHMANN F, KAUSHAL SP, GALANTE JO. Thromboembolic disease in patients undergoing total knee replacement. *Journal of Bone and Joint Surgery* 1976; **58A**: 928-32.
8. O'DONNELL TF, BREWSTER DC, DARLING RC, VEEN H, WALTMAN AA. Arterial injuries associated with fractures and/or dislocations of the knee. *Journal of Trauma* 1977; **17**: 775-84.
9. KAKKAR V. The diagnosis of deep vein thrombosis using the ¹²⁵I fibrinogen test. *Archives of Surgery* 1972; **104**: 152-9.
10. LEONARD RCF, NEVILLE E, HALL RJC. Paradoxical embolism. A review of cases diagnosed during life. *European Heart Journal* 1982; **3**: 362-70.
11. THOMPSON T, EVANS W. Paradoxical embolism. *Quarterly Journal of Medicine* 1930; **23**: 135-50.
12. NUNN JF. *Applied respiratory physiology*, 2nd edn. London: Butterworths, 1977: 255.
13. SCHULTE-SASSE U, HESS W, TARNOW J. Pulmonary vascular responses to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology* 1982; **57**: 9-13.
14. HUGHES JD, RUBIN LJ. Relation between mixed venous oxygen tension and pulmonary vascular tone during normoxic, hyperoxic and hypoxic ventilation in dogs. *American Journal of Cardiology* 1984; **54**: 1118-23.
15. HULL RD, RASKOB GE. Prophylaxis of venous thrombo-embolic disease following hip and knee surgery. *Journal of Bone and Joint Surgery* 1986; **68A**: 146-50.

Use of negative pressure ventilation to facilitate the return of spontaneous ventilation

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Summary

Negative pressure ventilation was used to facilitate the return of spontaneous ventilation in 10 patients with severe, chronic respiratory disability. All patients had required tracheal intubation and intermittent positive pressure ventilation, and conventional weaning techniques had failed. Details of the method are described. It permits extubation before spontaneous ventilation can be sustained indefinitely and thus assists the return of normal speech, sleep pattern and nutrition. The lack of flexible control of ventilatory variables and absence of access to the trachea for sputum clearance limit its widespread application.

Key words

Ventilation; mechanical, negative pressure.

Patients with chronic respiratory disability, particularly those with impaired ventilatory drive or the burden of greatly increased respiratory work, may have difficulty in the resumption of spontaneous breathing after a period of mechanical ventilation.¹ Respiratory insufficiency tends to recur during sleep even if satisfactory gas exchange is maintained by day, or to develop more insidiously if bronchial secretions cannot be cleared completely. Various techniques have been advocated to facilitate weaning from ventilatory support^{2,3} but most require some form of invasion of the airway, or application of a tightly fitting face-mask. The entirely non-invasive technique of negative pressure ventilation (NPV) is a suitable alternative in selected cases. We describe its use in 10 patients and comment on its advantages and limitations.

Clinical details

This report is based on the management of 10 consecutive patients (five male). Four were already inpatients at the Brompton Hospital and the remainder were transferred when conventional weaning techniques had failed. Four suffered from intrinsic pulmonary disease with at least some chronic airflow limitation (two emphysema, one cystic fibrosis, one sarcoidosis; mean forced expired volume in one second, 30% of predicted) and six were scoliotic (mean forced vital capacity 25% of value predicted according to span). Scoliosis was secondary to poliomyelitis in two cases and of idiopathic origin in four. Intermittent positive pressure ventilation (IPPV) had been required after thoracic

surgery in three patients (pleurectomy, Monaldi drainage of bullae and pneumonectomy, respectively) and the other seven received IPPV for acute respiratory failure, associated in four with evidence of respiratory tract infection. Details of the patients and the indications for IPPV are summarised in Table 1.

The mean duration of IPPV was 8.4 days (range 2–24 days). Attempts to restore spontaneous ventilation, which included the use of intermittent mandatory ventilation, had failed in all cases and several patients had been subjected to multiple trials of extubation. No patient had a tracheotomy, although this was under consideration as the next therapeutic manoeuvre in three cases. One already had a minitracheotomy but was still unable to maintain satisfactory spontaneous ventilation for more than 24–36 hours.

The procedure was explained to each patient, who was then transferred, still intubated, to a Cape Alligator or Kelleher tank ventilator. Both consist of a hinged cabinet which encloses the patient from the neck downwards; a seal round the neck is achieved with a soft rubber collar padded with gamgee to ensure comfort and prevent leaks. The two models differ in that the Kelleher allows the patient to be supported in a padded frame and then turned into the prone position to assist sputum clearance while ventilatory support is continued. This facility, although available, was not used in the present series. The tank ventilator operates at a negative pressure of up to -4 kPa and a respiratory rate which can be set at one of five values between 13 and 25 breaths/minute. The bellows pump

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Table 1. Subject data.

Patient	Age (years)	Underlying condition	Indication for IPPV	Duration of IPPV (days)
1	18	Cystic fibrosis	Postoperative pleurectomy	2
2	51	Emphysema	Postoperative Monaldi drainage of bullae	2
3	53	Pulmonary sarcoid	Postoperative right pneumonectomy	7
4	61	Emphysema	Respiratory tract infection	10
5	38	Congenital scoliosis, double-outlet right ventricle	Respiratory tract infection	3
6	64	Early onset idiopathic scoliosis	Acute respiratory failure	4
7	39	Paralytic scoliosis	Respiratory tract infection	8
8	51	Early onset idiopathic scoliosis	Acute respiratory failure	13
9	40	Congenital scoliosis	Acute respiratory failure	11
10	33	Paralytic scoliosis	Acute respiratory failure, possible respiratory tract infection	24

which evacuates the cabinet has a fixed inspiratory:-expiratory (I:E) ratio of 1:2.

Patients were extubated in the tank ventilator after a stabilisation period of between 30 minutes and 3-4 hours, during which time the rate and pressure settings were adjusted to optimise arterial blood gas tensions, and the effects of any residual sedatives were allowed to wane. The details of what would occur at extubation were explained to the patient while 100% oxygen was delivered through the tracheal tube. A port-hole on the tank was opened to prevent pharyngeal contents being sucked into the lungs as the intrathoracic pressure decreased during the ventilatory cycle; the tracheal tube cuff was then deflated and the tube withdrawn while continuous suction was applied through its lumen until it was clear of the mouth. Further suction within the mouth was necessary immediately afterwards before the port-hole could be closed safely and ventilation resumed. Humidified oxygen was delivered through nasal cannulae after extubation, although some patients with a predominantly extrapulmonary respiratory defect maintained satisfactory oxygenation while ventilated with air. Close supervision over the next 15-60 minutes ensured prompt suction within the mouth, either to clear saliva secreted after the stimulus of extubation or to remove bronchial secretions which some patients could cough into the pharynx. Thereafter, the volume of bronchial secretions diminished in most patients, and saliva was secreted in normal amounts and swallowed without difficulty. Most patients could whisper almost immediately and some could swallow with little or no difficulty; glottic function improved rapidly over a matter of hours in all patients. All slept for an hour or two after extubation and woke unconcerned by the physical constraints of the tank, and willing to accept further periods of treatment as required.

Arterial blood gas tensions were monitored by intermittent sampling and, in most cases, by continuous recording of transcutaneous carbon dioxide tension using a Hewlett-Packard Model 42701A capnograph. This, although not essential, helped to ensure that ventilatory settings were optimal; movement of the chest was more difficult to observe than usual, and the augmentation of tidal exchange by spontaneous breathing varied during the first few hours as anxiety and wakefulness waxed and waned. Other observations were kept to a minimum. Heart rate was

recorded manually from a superficial temporal pulse. Systemic pressure was measured only when the tank was opened for other nursing manoeuvres. Hourly urine output was recorded in patients who had a catheter in place at the time of transfer. Electrocardiograph leads, intravenous infusion lines and a urinary catheter can all be threaded through appropriate apertures in the body of the tank, but add obvious practical difficulties and predispose to air leaks from the cabinet.

The paucity of monitoring apparatus contrasts strikingly with the usual equipment of the intensive care unit and underlines the need to employ this technique only when the sole or major disability is respiratory and when other systems are stable and their function documented clearly at the outset. Frequent visits by an experienced observer, preferably one well known to the patient, are essential during the first 12-24 hours to ensure that any change is detected quickly. Patients usually regain considerable independence within this period and can report change themselves; encouraged by their own progress, they are often particularly responsive and explicit about how they feel.

Results

All 10 patients were extubated successfully and NPV was withdrawn progressively over approximately 2 weeks in six of them. The mean negative pressure required to maintain normocapnia was 2.2 kPa (range 1.6-3.0). No adverse haemodynamic events occurred and patients found the technique acceptable. Two patients developed copious purulent sputum associated with radiological evidence of pulmonary infection within a day or two of extubation. This, and the bouts of coughing which the sputum provoked, rendered ventilation inadequate and these patients were re-intubated, sedated and maintained on IPPV while the infection was controlled. One was subsequently weaned successfully using NPV and the other using positive pressure ventilation in the assist-control (triggered) mode with a Bird Mark 7 ventilator.

Two patients died within a few days of extubation, one from a peri-operative cerebrovascular accident and the other from terminal cardiorespiratory failure secondary to congenital heart disease and kyphoscoliosis. This patient was greatly distressed by intubation, IPPV and the intensive

care unit environment, especially since sedatives were prescribed sparingly while efforts were made to restore spontaneous ventilation. She was particularly grateful for the transition to noninvasive ventilatory support, even though she could sustain spontaneous ventilation only for short periods before respiratory distress recurred.

The remaining eight patients survived to leave hospital and are alive 11 months to 3 years later, although three have required domiciliary ventilatory support, again delivered noninvasively, to control nocturnal hypoventilation.

Discussion

These cases demonstrate that NPV can be used successfully to facilitate the resumption of spontaneous ventilation when other methods have failed. It is indicated particularly for patients with chronic, stable but severe respiratory disability in whom an acute and potentially reversible event has precipitated the need for mechanical ventilation. Even when the antecedent acute event has been treated successfully, the return of spontaneous ventilation is prevented by the erosion of their marginal functional reserves by recent illness, sleep disturbance and interference with enteral nutrition, as well as by the increase in bronchial secretions and impairment of clearance mechanisms which result from tracheal intubation. Tracheostomy eliminates some but not all of these difficulties, and introduces mechanical hazards which occur more often in patients with deformity of the thoracic cage or airway.

The tank ventilator provides a means to assist ventilation without invasion of the airway. No sedation is required, essential monitoring can be kept to a minimum and so there is less need for disturbance. Patients can eat, drink and speak normally, and natural sleep patterns are re-established. This aids mobilisation and boosts morale, especially for patients who are depressed and frightened by repeated unsuccessful attempts to breathe spontaneously.

The provision of ventilatory support maintains normocapnia and prevents the development of a compensatory metabolic alkalosis, and thus preserves the sensitivity of the hypercapnic ventilatory response.⁴ Sleep-related disturbances of breathing are eliminated and this helps to prevent the development or worsening of pulmonary hypertension⁵ and consequent right heart failure. Respiratory muscle fatigue is difficult to quantify but it probably contributes also to the pathogenesis of respiratory failure in patients in whom the work of breathing is increased. A reduction in diaphragmatic electromyographic activity to 9% (SD 3%) of the value recorded during spontaneous ventilation was reported by Rochester *et al.*⁶ when NPV was used to treat patients with respiratory failure of varying aetiology. Respiratory muscle rest allows subsequent periods of spontaneous ventilation to be undertaken with strength and endurance at their best.⁷ Respiratory muscle fatigue is also diminished by prevention of sleep deprivation. Breathless patients are often unable to sleep because the consequent reduction in tone of diaphragm, intercostal and, above all, accessory muscles, leads to hypoventilation and thence arousal in response to hypoxaemia and hypercapnia.⁸ At the same time, respiratory muscle function is compromised by hypercapnia⁹ and hypoxaemia,^{10,11} and hypercapnic ventilatory drive is impaired by sleep deprivation.¹²

The provision of ventilatory support without invasion of the airway offers the advantages enumerated above but can be used safely only in patients with intact airway reflexes who can clear their own bronchial secretions, aided if necessary by percussion, drainage and assisted coughing. Tracheostomy, or even a minitracheostomy, makes clearance of secretions easier but prevents the collar on the tank ventilator from fitting comfortably and sealing easily. These should be avoided in patients who are considered for NPV; not only does this facilitate use of the tank, but it also eliminates any immediate or long-term hazard to the trachea and means that the stimulus to bronchial hypersecretion and an obvious portal of entry for pathogens into the respiratory tract are eliminated with removal of the tracheal tube.

The provision of ventilatory support for all but a few moments during and immediately after the manoeuvre of extubation compensates for the increased ventilatory requirements of coughing, swallowing and re-acclimatisation to a natural airway which is often compromised at first by a degree of laryngeal oedema. A major disadvantage of the technique is that patients are extubated while supine, so that secretions in the pharynx are likely to be aspirated into the lungs when the intrathoracic pressure decreases with the onset of the inspiratory cycle. This risk is minimised by extubating only when the patient is fully conscious, and subsequent meticulous attention to the immediate removal of secretions from the mouth, particularly during the first few hours while glottic function recovers. Patients cannot be turned rapidly while in the tank, and any threat of aspiration from the pharynx should be treated not only by immediate suction but also by opening a porthole to eliminate the negative pressure within the cabinet. For similar reasons, an empty stomach and functioning gastrointestinal tract are also prerequisites for safe extubation with this technique. A careful explanation of what is entailed helps to allay anxiety both initially and during the manoeuvre of extubation.

Essential nursing procedures are best carried out with the tank open unless nursing expertise and experience are exceptional. This means that patients should be able to sustain spontaneous ventilation for 10–15 minutes at a time before the method is attempted. Provision of a portable bed-rest which fits into the open tank means that patients can remain upright without effort while they breathe spontaneously.

The degree of control of ventilatory variables during NPV is extremely limited. Provided that a satisfactory negative pressure can be achieved, this inflexibility is rarely a handicap when patients with extrapulmonary disease are ventilated but it is a considerable disadvantage for those with intrinsic pulmonary disease. Severe or variable airflow limitation can make it impossible to secure satisfactory gas exchange and may cause considerable air trapping, and so the technique cannot be recommended in these circumstances.

The limited availability of appropriate equipment restricts the widespread application of NPV and it is the method of choice in only a small number of patients. The recent resurgence of interest in the applications of NPV^{13–15} and the distribution by the DHSS of two batches, each of 10 tank ventilators, to selected centres in the U.K. warrants an awareness of the benefits and limitations of their use.

References

1. BRANTHWAITE MA. Acute on chronic respiratory failure. *Clinics in Anaesthesiology* 1985; **3**: 831-47.
2. BROWNE DRG. Weaning patients from mechanical ventilation. *Intensive Care Medicine* 1984; **10**: 55-8.
3. MATTHEWS HR, HOPKINSON RB. Treatment of sputum retention by minitracheotomy. *British Journal of Surgery* 1984; **71**: 147-50.
4. FENCL V, VALE JR, BROCH JA. Respiration and cerebral blood flow in metabolic acidosis and alkalosis in humans. *Journal of Applied Physiology* 1969; **27**: 67-76.
5. BOYSEN PG, BLOCK AJ, WYNNE JW, HUNT LA, FLICK MR. Nocturnal pulmonary hypertension in patients with chronic obstructive pulmonary disease. *Chest* 1979; **76**: 536-42.
6. ROCHESTER DF, BRAUN NMT, LAINE S. Diaphragmatic energy expenditure in chronic respiratory failure. The effect of assisted ventilation with body respirators. *American Journal of Medicine* 1977; **63**: 223-32.
7. BRAUN NMT, MARINO WD. Effect of daily intermittent rest of respiratory muscles in patients with severe chronic airflow limitation (CAL). *Chest* 1984; **85**: 59S.
8. FLEETHAM J, WEST P, MEZON B, CONWAY W, ROTH T, KRYGER M. Sleep, arousals, and oxygen desaturation in chronic obstructive pulmonary disease. The effect of oxygen therapy. *American Review of Respiratory Disease* 1982; **126**: 429-33.
9. JUAN G, CALVERLEY P, TALAMO C, SCHNADER J, ROUSSOS C. Effect of carbon dioxide on diaphragmatic function in human beings. *New England Journal of Medicine* 1984; **310**: 874-9.
10. ROUSSOS C, MACKLEM PT. Diaphragmatic fatigue in man. *Journal of Applied Physiology* 1977; **43**: 189-97.
11. JARDIM J, FARKAS G, PREFAUT C, THOMAS D, MACKLEM PT, ROUSSOS C. The failing inspiratory muscles under normoxic and hypoxic conditions. *American Review of Respiratory Disease* 1981; **124**: 274-9.
12. COOPER KB, PHILLIPS BA. Effect of short-term sleep loss on breathing. *Journal of Applied Physiology* 1982; **53**: 855-8.
13. GARAY SM, TURINO GM, GOLDRING RM. Sustained reversal of chronic hypercapnia in patients with alveolar hypoventilation syndromes. Long-term maintenance with noninvasive nocturnal mechanical ventilation. *American Journal of Medicine* 1981; **70**: 269-74.
14. DUNKIN LJ. Home ventilatory assistance. *Anaesthesia* 1983; **38**: 644-9.
15. SAWICKA EH, BRANTHWAITE MA, SPENCER GT. Respiratory failure after thoracoplasty: treatment by intermittent negative-pressure ventilation. *Thorax* 1983; **38**: 433-5.

Spinal haematoma following epidural analgesia

Report of a patient with ankylosing spondylitis and a bleeding diathesis

H. GUSTAFSSON, H. RUTBERG AND M. BENGTSSON

Summary

A patient who developed an epidural haematoma with multifactorial aetiology (bleeding diathesis, ankylosing spondylitis, chronic alcoholism and acute pancreatitis) after epidural analgesia for pain relief is described. Our conclusion is that adequate laboratory screening of blood coagulation, including platelet count, should be carried out in this category of patient before attempted epidural blockade, the risks of which must be weighed against the benefits. The block should be allowed to wear off intermittently and repeated neurological assessment performed if an epidural catheter is used for repeated injections or for a continuous infusion of local anaesthetic. Neuroradiological examination should be carried out promptly if an epidural haematoma is suspected and surgical decompression performed without delay if the diagnosis is confirmed.

Key words

Anaesthetic techniques; regional; epidural.

Spinal cord; paraplegia.

Serious neurological sequelae following epidural analgesia are rare; in the literature the incidence of paraplegia is less than 1 in 10 000 procedures.^{1–2} Several factors may contribute to postepidural paraplegia,^{3,4} one of which is epidural haemorrhage with the development of an epidural haematoma. In this case report, we highlight the risks of developing an epidural haematoma with paraplegia, when epidural analgesia is administered in a patient with a bleeding diathesis and especially in the presence of ankylosing spondylitis.

Case history

A 46-year-old man with abdominal pain was admitted as an emergency to a district hospital. The preliminary diagnosis was acute pancreatitis, following a period of heavy alcohol consumption. He was a chronic alcoholic and had been treated several times for recurrent pancreatitis which had ended in pancreatic insufficiency and diabetes mellitus. Except for insulin he was receiving no other medication. He also suffered from ankylosing spondylitis. There was no known tendency to bleed. His temperature on admission was 38.6°C, his circulatory condition stable with an arterial blood pressure of 180/100 mmHg and pulse rate 95–110 beats/minute. Laboratory tests showed that haemoglobin, haematocrit, white blood cell count, serum sodium, potassium, creatinine and urinary amylase were within normal

limits. Standard liver tests indicated slightly impaired liver function. A prothrombin complex test was 95% (normal range 70–130%).

It was decided to use epidural analgesia to provide adequate pain relief. At 19:45 hours an 18-gauge Tuohy needle was introduced through the T_{11–12} interspace via a midline puncture using a loss of resistance technique. Minor bleeding was noticed but otherwise there were no difficulties. An epidural catheter was introduced in a cephalad direction with the tip approximately 3 cm into the space. No blood could be aspirated through the catheter. Six millilitres of 0.5% bupivacaine were injected and produced good pain relief. A continuous infusion of 0.25% bupivacaine at 5 ml/hour was started and continued through the night. An indwelling urinary catheter was inserted for measurement of urine output.

The next morning, at about 07:30 hours, the patient complained of a total inability to move his legs. The bupivacaine infusion was stopped at 09:00 hours in order to evaluate the patient's abdominal status. In the early afternoon, a flaccid paralysis with areflexia of both legs and loss of sensibility to cold below T₁₀ on the right side and below L₁ on the left side was noted. The prothrombin complex test was now 55%, the platelet (thrombocyte) count $72 \times 10^9/\text{litre}$ (normal range $140\text{--}400 \times 10^9/\text{litre}$) and activated partial thromboplastin time (APTT) normal. Vitamin K 10 mg was given and the epidural catheter

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removed; significant bleeding was observed through the hole of insertion, which necessitated compression. The patient was then transferred to our university hospital. Thoracolumbar myelography at 22:50 hours (about 27 hours after epidural puncture) revealed an expansive process that started at the lower level of L₁ with a complete block to the passage of contrast medium above T₁₂. A further prothrombin screen test and APTT were within the normal range. The platelet count was only $51 \times 10^9/\text{litre}$ and bleeding time (IVY) was >2100 seconds (normal range 120–630 seconds). The patient was given fresh frozen plasma and platelets. About 29 hours after the epidural puncture a T_{10–12} laminectomy was performed and an epidural haematoma that extended from T₉–L₁ was removed.

The patient regained full sensation a few days later with an increasing ability to move his legs. He still had some paresis in his legs 10 days postoperatively but it was possible to mobilise him with support. Attempts to remove the indwelling urinary catheter were unsuccessful because of a bladder paresis. The patient was able to walk with the aid of a cane about one month postoperatively. His bladder paresis had regressed markedly and the indwelling urinary catheter could be removed.

Discussion

This case report illustrates some details to be considered before the commencement of epidural analgesia and in its subsequent management. Spinal epidural and intradural haemorrhage with haematoma formation may develop spontaneously both in patients who do not receive anticoagulants^{5–7} and in those who do.^{7–10} Other causes include intradural or epidural puncture or catheterisation, especially in association with ongoing or subsequent anticoagulant therapy.^{11–19} Removal of an epidural catheter before reversal of anticoagulation has also been associated with this problem.^{12,13,19} Treatment with aspirin and other drugs with antiplatelet effects may contribute to the occurrence of an intraspinal haemorrhage^{20–22} and the issue as to when intradural or epidural blocks can be safely performed on patients treated with such drugs, remains to be further elucidated.^{23,24}

Blood vessel puncture with needle or catheter is the most common complication of epidural analgesia. Figures between 2.8% and 11.5% are quoted in the literature.^{1,25,26} With this in mind and because of the risk of devastating effects should a haematoma develop, it is generally considered that anticoagulant therapy is a contraindication to intradural or epidural analgesia.^{27,28} Even the use of low dose heparin pre-operatively has been questioned, since there is a lack of data to confirm its safety.^{17,29} There were no reported cases to suggest the presence of a spinal haematoma in one small series of 187 patients who received pre- and postoperative low dose (5000 IU) heparin with dihydroergotamine and who were operated upon under spinal or epidural analgesia.³⁰ It should be remembered that plasma heparin levels 2 hours after injection may be high in some patients who receive subcutaneous low dose heparin, with the risk of increased bleeding.³¹ The combination of low dose heparin and dextran as a plasma expander should be avoided because of a definite increased tendency to bleed.³²

Epidural analgesia has been advocated as a safe method

in patients who receive anticoagulant therapy provided that those with thrombocytopenia, prothrombin complex test below 10%, long-standing aspirin therapy and heparinisation prior to epidural block are excluded.³³ Furthermore, the use of a midline puncture technique with a lower risk of vessel puncture is advocated.^{23,33} Even the commencement of anticoagulation with heparin following placement of an epidural or subarachnoid catheter has been reported as a safe technique provided that patients are properly selected, no blood vessel is punctured, anticoagulant activity is monitored and plasma heparin levels are low when the catheter is removed.^{33–35}

Abnormal haemostasis due to a deficiency of coagulation factors and platelets could be expected in this particular case, a chronic alcoholic with presumptive liver disease and secondary hypersplenism. In addition, ethanol itself in large amounts suppresses haematopoiesis, including thrombopoiesis.³⁶ Furthermore, increased intra-abdominal pressure due to ascites may divert blood into the epidural veins, which become distended. We believe that in our case chronic alcoholism may have contributed to the development of the haematoma since spontaneous haematoma and those caused by spinal puncture have been described in such patients.^{37,38}

Patients with acute pancreatitis are prone to develop disturbances in the proteolytic enzyme systems, and reduced platelet counts which produce potential bleeding abnormalities.³⁹ The lowest platelet value recorded in this patient was $51 \times 10^9/\text{litre}$ and the bleeding time (IVY) indefinite. It is advisable that a platelet count and, if possible, a bleeding time and a screen of the prothrombin complex should be performed in alcoholics and in patients with acute pancreatitis before attempted intradural or epidural blockade.

A difficult back with associated difficult puncture due to abnormalities of the spine or spinal canal, is a known cause of paraplegia following epidural analgesia.^{2,17,22,40,41} An unrecognised problem concerns this patient's pathology of the spine. Ankylosing spondylitis makes the spine both stiff and brittle. Puncture of the epidural or subarachnoid spaces is sometimes impossible because of extensive intervertebral calcification. In the reported case bleeding occurred when the needle entered the epidural space. Inflammatory changes within and around the intervertebral foramina may create a confined space and hamper the leakage of blood out of the epidural space.^{42,43} Bleeding in the epidural space in such a patient might, therefore, have a much more dramatic effect than normally seen.^{44–47}

Another point of interest is that of how epidural analgesia with local anaesthetics should be managed in a patient with increased risk of developing bleeding in the epidural space. In our opinion, the blockade should be allowed to wear off intermittently and we therefore prefer repeated injections with careful neurological examination of motor and sensory function before each top-up dose, rather than a continuous infusion technique. Radiating back pain, sensory changes and muscular weakness that progresses towards paraplegia should arouse suspicion of an epidural haematoma. Neuroradiological examination and decompressive surgery must then be promptly performed. In this case the patient had almost complete recovery, although about 29 hours elapsed between the start of epidural bleeding (time of epidural puncture) and evacuation of the haematoma.

References

1. DAWKINS CJM. An analysis of the complications of extradural and caudal block. *Anaesthesia* 1969; **24**: 554-63.
2. USUBIAGA JE. Neurological complications following epidural anesthesia. *International Anesthesiology Clinics* 1975; **13**: 1-153.
3. KANE RE. Neurologic deficits following epidural or spinal anesthesia. *Anesthesia and Analgesia* 1981; **60**: 150-61.
4. SKOUEN JS, WAINAPEL SF, WILLOCK MM. Paraplegia following epidural anesthesia. A case report and a literature review. *Acta Neurologica Scandinavica* 1985; **72**: 437-43.
5. LOUGHEED WM, HOFFMAN HJ. Spontaneous spinal extradural hematoma. *Neurology* 1960; **10**: 1059-63.
6. MARKHAM JW, LYNDE HN, STAHLMAN GEB. The syndrome of spontaneous spinal epidural hematoma. Report of three cases. *Journal of Neurosurgery* 1967; **26**: 334-42.
7. COSTABILE G, HUSAG L, PROBST C. Spinal epidural hematoma. *Surgical Neurology* 1984; **21**: 489-92.
8. SPURNY OM, RUBIN S, WOLF JW, WU WQ. Spinal epidural hematoma during anticoagulant therapy. *Archives of Internal Medicine* 1964; **114**: 103-7.
9. HARIK SI, RAICHEL ME, REIS DJ. Spontaneously remitting spinal epidural hematoma in a patient on anticoagulants. *New England Journal of Medicine* 1971; **284**: 1355-7.
10. BAMFORD CR. Spinal epidural hematoma due to heparin. LETTER. *Archives of Neurology* 1978; **35**: 693-4.
11. HELPERIN SW, COHEN DD. Hematoma following epidural anesthesia: report of a case. *Anesthesiology* 1971; **35**: 641-4.
12. DEANGELIS J. Hazards of subdural and epidural anesthesia during anticoagulant therapy: a case report and review. *Anesthesia and Analgesia* 1972; **51**: 676-9.
13. JANIS KM. Epidural hematoma following postoperative epidural analgesia: a case report. *Anesthesia and Analgesia* 1972; **51**: 689-92.
14. VARKEY GP, BRINDLE GF. Peridural anaesthesia and anticoagulant therapy. *Canadian Anaesthetists' Society Journal* 1974; **21**: 106-9.
15. SADJADPOUR K. Hazards of anticoagulation therapy shortly after lumbar puncture. *Journal of the American Medical Association* 1977; **237**: 1692-3.
16. BREM SS, HAFER DA, VAN UITERT RL, RUFF RL, REICHERT WH. Spinal subarachnoid hematoma. A hazard of lumbar puncture resulting in reversible paraplegia. *New England Journal of Medicine* 1981; **304**: 1020-1.
17. OWENS EL, KASTEN GW, HESSEL EA. Spinal subarachnoid hematoma after lumbar puncture and heparinization: a case report, review of the literature, and discussion of anesthetic implications. *Anesthesia and Analgesia* 1986; **65**: 1201-7.
18. GINGRICH TF. Spinal epidural hematoma following continuous epidural anesthesia. *Anesthesiology* 1968; **29**: 162-3.
19. BUTLER AB, GREEN CD. Haematoma following epidural anaesthesia. *Canadian Anaesthetists' Society Journal* 1970; **17**: 635-9.
20. LOCKE GE, GIORGIO AJ, BIGGERS SL, JOHNSON AP, SALEM F. Acute spinal epidural hematoma secondary to aspirin-induced prolonged bleeding. *Surgical Neurology* 1976; **5**: 293-6.
21. GREENSTE FS, KATZ J. Spinal subdural hematoma associated with attempted epidural anesthesia and subsequent continuous spinal anesthesia. *Anesthesia and Analgesia* 1980; **59**: 72-3.
22. MAYUMI T, DOHI S. Spinal subarachnoid hematoma after lumbar puncture in a patient receiving antiplatelet therapy. *Anesthesia and Analgesia* 1983; **62**: 777-9.
23. BENZON HT, BRUNNER EA, VAISRUB N. Bleeding time and nerve blocks after aspirin. *Regional Anesthesia* 1984; **9**: 86-9.
24. HINDMAN BJ, KOKA BV. Usefulness of the post-aspirin bleeding time. *Anesthesiology* 1986; **64**: 368-70.
25. VERNIQUET AJW. Vessel puncture with epidural catheters. Experience in obstetric patients. *Anaesthesia* 1980; **35**: 660-2.
26. BECK H, BRASSOW F, DOEHN M, BAUSE H, DZIADZKA A, SCHULTE AM, ESCH J. Epidural catheters of the multi-orifice type: dangers and complications. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 549-55.
27. UPPINGTON J. Anesthetic management of patients with coagulation disorders. *International Anesthesiology Clinics* 1985; **23**: 125-40.
28. VANDAM L. Neurological sequelae of spinal and epidural anesthesia. *International Anesthesiology Clinics* 1985; **24**: 231-55.
29. MATTINGLY SB, STANTON-HICKS M. Low-dose heparin therapy and spinal anesthesia. Questions and answers. *Journal of the American Medical Association* 1981; **246**: 886.
30. ALLEMANN BH, GERBER H, GRUBER UF. Rückenmarksnahe Anaesthetie und subkutan verabreichtes low-dose Heparin-Dihydroergot zur Thromboembolieprophylaxe. (Perispinal anesthesia and subcutaneous administration of low-dose heparin-dihydroergot for prevention of thromboembolism.) *Anaesthesist* 1983; **32**: 80-3.
31. BROZOVIC M, STIRLING Y, ABBOSH J. Plasma heparin levels after low dose subcutaneous heparin in patients undergoing hip replacement. *British Journal of Haematology* 1975; **31**: 461-6.
32. KORTTILA K, LAURITSALO K, SÄRMÖ A, GORDIN A, SUNDBERG S. Suitability of plasma expanders in patients receiving low-dose heparin for prevention of venous thrombosis after surgery. *Acta Anaesthesiologica Scandinavica* 1983; **27**: 104-7.
33. ODOM JA, SIH IL. Epidural analgesia and anticoagulant therapy. Experience with one thousand cases of continuous epidurals. *Anaesthesia* 1983; **38**: 254-9.
34. MCCULLOUGH JD, STANLEY TH, LUNN JK. Anticoagulants and continuous epidural anesthesia. LETTER. *Anesthesia and Analgesia* 1980; **59**: 394-5.
35. RAO TLK, EL-ETR AA. Anticoagulation following placement of epidural and subarachnoid catheters: an evaluation of neurologic sequelae. *Anesthesiology* 1981; **55**: 618-20.
36. SULLIVAN LW, HERBERT V. Suppression of hematopoiesis by ethanol. *Journal of Clinical Investigation* 1964; **43**: 2048-62.
37. LONDON GW, MCKEEVER PE, WIEDERHOLT WC. Spontaneous spinal epidural hematoma in alcoholism. *Annals of Internal Medicine* 1974; **81**: 266-7.
38. DUNN D, DHOPESH V, MOBINI J. Spinal subdural hematoma. A possible hazard of lumbar puncture in an alcoholic. *Journal of the American Medical Association* 1979; **241**: 1712-3.
39. AASEN AO, KIERULF P, RUUD TE, GODAL HC, AUNE S. Studies on pathological plasma proteolysis in patients with acute pancreatitis. A preliminary report. *Acta Chirurgica Scandinavica* 1982; **509** (Suppl.): 83-7.
40. BALLIN NC. Paraplegia following epidural analgesia. *Anaesthesia* 1981; **36**: 952-3.
41. STEPHANOV S, DE PREUX J. Lumbar epidural hematoma following epidural anesthesia. *Surgical Neurology* 1982; **18**: 351-3.
42. BATSON OV. The function of the vertebral veins and their role in the spread of metastases. *Annals of Surgery* 1940; **112**: 138-49.
43. MOORE DC. *Complications of regional anesthesia. Etiology, signs and symptoms, treatment.* Oxford: Blackwell Scientific Publications, 1955.
44. AGNETTI V, MONACO F, MUTANI R. Post-convulsive spinal epidural haematoma in ankylosing spondylitis. *European Neurology* 1979; **18**: 230-3.
45. BYNKE O, JOHANSSON K-E, SÖKJER H. Intraspinal epidural hematoma - en vanlig komplikation vid epiduralanestesi. (Intraspinal epidural hematoma - an unusual complication in epidural anesthesia.) *Läkartidningen* 1985; **82**: 1772, 1774.
46. LESOIN F, CAMA A, LOZES G, JOMIN M. Hématome extradural cervical post-traumatique chez un malade atteint de spondylarthrite ankylosante. (Post-traumatic extradural cervical hematoma in a patient with ankylosing spondylarthritis.) *La Presse Médicale* 1985; **14**: 1429-30.
47. HISSA E, BOUMPHREY F, BAY J. Spinal epidural hematoma and ankylosing spondylitis. *Clinical Orthopaedics and Related Research* 1986; **208**: 225-7.

CASE REPORT

HELLP syndrome and the anaesthetist

B. L. DUFFY

Summary

Four pregnant patients are described who had varying signs of pre-eclampsia plus haemolysis, elevated liver enzymes and a low platelet count. Two of the patients presented without hypertension and all posed considerable diagnostic difficulties, with problems in clinical management. Pregnancy induced hypertension is only one manifestation of a much more diverse pathophysiological process. Anaesthetists need to be aware of these other pregnancy related disorders in order to avoid diagnostic pitfalls and to enable them to provide safely the appropriate general and regional anaesthetic techniques.

Key words

Blood coagulation; thrombocytopenia.

Liver; hepatitis.

Pregnancy; pre-eclampsia.

Hypertensive disease of pregnancy complicates up to 10% of all pregnancies and is responsible for increased maternal and perinatal mortality and morbidity.¹ A unique group of pre-eclamptic/eclamptic patients was recently described with the associated findings of haemolysis, elevated liver enzymes and low platelet count (HELLP syndrome).² There is debate whether this syndrome is a distinct entity³ and whether aggressive management with urgent delivery is always required,⁴ but there is no doubt that some pregnant women present with a complicated picture of diverse clinical signs and symptoms, unlike the classical presentation of pre-eclampsia. Many of these patients are extremely ill.

In a matter of a few months we were presented with four pregnant women who had all or some of the features of the HELLP syndrome. These patients are described, as are some of the difficulties which may be experienced by anaesthetists involved in their care.

Case histories

Case 1

A 27-year-old woman in her first pregnancy had an uneventful antenatal course until 38 weeks' gestation when she was admitted for rest and investigation because of an arterial blood pressure of 130/90 mmHg, oedema, proteinuria and haematuria. The blood picture showed her haemoglobin to be 12.1 g/dlitre, platelet count 140 000/ml (normal range 150–400 000) and crenated blood cells in the blood

film that suggested haemolysis. Blood chemistry revealed an elevated uric acid of 522 μ mol/litre (normal range 150–300) and elevated levels of aspartate aminotransferase (AST), 97 units/litre and alanine aminotransferase (ALT), 212 units/litre (normal ranges 0–45). A diagnosis was made of worsening pre-eclampsia with possible development of the HELLP syndrome. Labour was induced with vaginal prostaglandins. The arterial pressure increased on one occasion to 155/90 mmHg but was mostly recorded at 130/80 mmHg.

She was commenced on phenobarbitone 200 mg 6-hourly by intravenous injection as a prophylactic anticonvulsant. The coagulation screen was normal and the platelet count was now 184 000/ml so lumbar epidural analgesia was provided on request. Delivery was eventually achieved by rotational forceps and blood loss was recorded as 250 ml. The patient's condition remained satisfactory; diuresis commenced after delivery and arterial blood pressure remained at normal levels. However, 30 hours postpartum she was pale, dyspnoeic and had signs of consolidation in the left lower lobe with crepitations in both lungs. The haemoglobin now was 7.6 g/dlitre and the platelet count 66 000/ml. The arterial pressure had increased to 160/80 mmHg and she had exaggerated tendon reflexes with ankle clonus. Blood transfusion was commenced while transfer to the intensive care unit was organised. The chest radiograph was very suggestive of adult respiratory distress syndrome (ARDS). In the intensive care unit an F_{IO_2} of 0.5 was required to achieve a P_{aO_2} greater than 8 kPa. It was necessary to transfuse 8 units of blood over 4 days to

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maintain a satisfactory haemoglobin level. Haemolysis was confirmed by the appearance of the blood film and by considerably reduced haptoglobin levels. The liver function tests remained elevated for over a week but gradually improved. Her lung function slowly returned to normal but at discharge the hypertension which developed postpartum still required treatment.

Case 2

This 28-year-old mother was in her second pregnancy; she had one previous termination of pregnancy. Her antenatal course was uneventful apart from an occasional trace of protein in the urine. A reduced platelet count of 139 000/ml at 39 weeks' gestation was recorded in the antenatal clinic but no action was taken. She was admitted at 41 weeks with an arterial blood pressure of 150/80 mmHg, proteinuria, oedema and increased reflexes. Investigations now revealed a haemoglobin level of 11.9 g/dlitre, platelet count 77 000/ml, a markedly elevated uric acid level and a mild increase of liver function tests.

Vaginal prostaglandins were inserted to ripen the cervix and labour was induced the following day. The coagulation screen was absolutely normal apart from a platelet count of 70 000/ml. Lumbar epidural block was contraindicated by the thrombocytopenia so conventional analgesia of pethidine and nitrous oxide inhalation was used. Phenobarbitone 200 mg was given intravenously every 4 hours to prevent convulsions. During labour the arterial pressure increased occasionally to 160/90 mmHg but generally was at satisfactory levels. Eventually the patient delivered a healthy infant and blood loss was recorded as 300 ml. She remained well until next day when intravenous hydralazine was required for the control of hypertension. The haemoglobin level had decreased to 9.5 g/dlitre, the platelet count had fallen further to 53 000/ml and there was continued slight elevation of liver function tests. In the absence of obvious blood loss it was assumed that haemolysis was occurring. Two units of whole blood were transfused. The arterial pressure settled over the next 3 days and the haemoglobin level and platelet count returned to normal.

Case 3

This 35-year-old mother was pregnant with twins in her second pregnancy. She was admitted for induction of labour at 38 weeks gestation at which time her arterial blood pressure was 130/60 mmHg and she had pitting oedema that extended to her knees. Lumbar epidural analgesia was requested following artificial rupture of the membranes. An attempt at L_{2/3} was unsuccessful, but an epidural catheter was inserted without difficulty at L_{3/4} and satisfactory analgesia achieved. The first skin puncture site was now noticed to be oozing continuously and a coagulation screen was performed. The platelet count was 74 000/ml, the activated partial thromboplastin time (APTT) 35 seconds (normal range 22–34) and fibrin degradation products (FDP) were 19.2 µg/ml (normal <8). Since the epidural block was well established and no blood was visible in the epidural catheter on aspiration, a decision was made to leave the catheter in place. Her ability to perform leg movements was confirmed before each top-up was administered. Subsequent results showed a high uric acid level, mild elevation of liver function tests and a markedly

reduced albumin level which probably contributed to the peripheral oedema.

The arterial blood pressure remained at 130/60 mmHg throughout labour, at the end of which she was delivered of healthy twins. The epidural block was of immense value in the manipulation and delivery of the second twin. On the advice of a haematologist she was given 6 packs of platelets postpartum to prevent haemorrhage from the large placental site. As it turned out she had a moderate vaginal loss but the greatest cause of concern was the continued oozing from the original epidural puncture site. This required frequent dressing changes and application of pressure. No neurological sequelae developed. On the day after delivery the haemoglobin level had decreased by 2 g/dlitre and the platelet count was 78 000/ml. She did not receive a transfusion and by day 4 the platelet count was 145 000/ml.

Case 4

This 23-year-old mother in her third pregnancy was admitted at 36 weeks gestation when she felt and looked unwell, with complaints of left flank pain. Her arterial blood pressure was 100/60 mmHg. A urinary tract infection was suspected but subsequent investigations revealed a markedly elevated uric acid level, a total bilirubin of 70 µmol/litre (normal range 1–20) and elevation of all liver enzymes. In particular, there was gross elevation of AST, 786 units/litre and ALT, 969 units/litre.

Infectious hepatitis was now thought to be the most likely diagnosis and barrier nursing was instituted while further investigations were undertaken. A battery of tests failed to find an infectious cause for the hepatic derangement. An ultrasound examination did not show any gall stones. The disturbed liver function was confirmed by a grossly abnormal coagulation screen. The prothrombin activity was 18%, the APTT 81 seconds and fibrinogen level 0.4 g/litre. The platelet count was only mildly depressed at 142 000/ml.

She was given vitamin K parenterally but on the next day, by the time she went into spontaneous labour the prothrombin activity was 10%, the APTT was greater than 300 seconds and the fibrinogen level was 0.13 g/litre. Six units of fresh frozen plasma and 2 units of cryoprecipitate were infused. She had a spontaneous vaginal delivery of an infant which initially required resuscitation but then did well. A retained placenta was removed using nitrous oxide analgesia. The coagulation parameters improved after delivery but the platelet count was now 84 000/ml.

There was a large postpartum haemorrhage the following day which required blood transfusion and more fresh frozen plasma. Further improvement occurred the next day although the platelet count decreased to 59 000/ml. Subsequently there was slow, gradual improvement but she remained jaundiced for over a week and the liver function tests suggested more of a cholestatic picture. At last report the jaundice had resolved and the liver function tests were returning to normal.

Discussion

Pre-eclampsia has many presentations that include variations on the well-known triad of hypertension, proteinuria and oedema. The association of haematological abnormalities with pre-eclampsia and eclampsia has been known

for some time.^{5,6} In 1982, Weinstein² described a subgroup of patients in whom the added features of haemolysis, elevated liver enzymes and low platelet count were also present. Other findings of note were that the hypertension was not always severe and the coagulation changes were essentially of thrombocytopenia, not disseminated intravascular coagulation. The first patient fits this description very well, with the added complication of adult respiratory distress syndrome which is a rare but previously described accompaniment.⁷

The second case had only moderate hypertension with a slight elevation of liver function tests. There was a marked thrombocytopenia of 70 000/ml and the decreased haemoglobin level in the absence of external blood loss was consistent with haemolysis.

The third patient was never hypertensive at any time. She had mild elevation of liver function tests but the main feature was a thrombocytopenia with, possibly, a low grade disseminated intravascular coagulopathy. The problem from the anaesthetist's point of view was that the epidural catheter was inserted before the coagulation test results were available. In fact, these tests were performed because of continual oozing from an epidural skin puncture site. Fortunately, no spinal cord compression occurred but close monitoring of neurological function was instituted. This case also raises the question of what screening procedures should be performed in cases which are anticipated to be without difficulty. What is an adequate number of platelets to be accepted before regional anaesthesia is undertaken? The generally accepted figure of 100 000/ml may be too low, particularly if platelet function is not known. Is a platelet count sufficient or should a bleeding time also be determined?

The final patient presented a bizarre picture in which the markedly elevated uric acid level was indicative of a pre-eclamptic process but where there was gross and serious liver disturbance. This really fits into the category of gestosis, or expanded toxemia syndrome, described by Goodlin.³ He considers the current definition of pre-eclampsia to have become too restrictive. It does not take into account the polysymptomatic diseases that involve multiple target organs which can occur in pregnancy. These disorders have been known for over 100 years and usually have the same underlying pathological mechanism. A series of patients similar to our fourth patient has been described with major liver function disturbances but without hypertension or proteinuria.⁸ Liver biopsies showed the classical pre-eclamptic histopathological changes of periportal inflammatory infiltration and large fibrin deposits in the hepatic sinusoids. In cases such as this other diagnoses are often made, for example hepatitis or cholelithiasis, and inappropriate treatment may be instituted. Fortunately, experience with the previous patients alerted us to the pos-

sibility of a pregnancy related condition, although it was necessary initially to nurse her as if she had an infectious hepatitis until test results were available. A potential problem for the anaesthetist concerns the effect of a general anaesthetic on the already severely disturbed liver function. Regional anaesthesia could not be considered because of the depressed level of coagulation factors.

The existence of the HELLP and other related syndromes needs to be borne in mind by anaesthetists and by their obstetric colleagues. Some of the patients are seriously ill; liver rupture with death has been reported.⁶ Management is often complicated and transfer to intensive care units may be required. Classical pre-eclampsia is probably just one presentation of a much more diverse and widespread pathophysiological disturbance. Fortunately, all of these pregnancy related conditions are cured by delivery, although not always immediately and, sometimes, not before a serious deterioration in the clinical condition.

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References

1. GOLDBRAND JW, FUENTES AM. The relation of angiotensin-converting enzyme to the pregnancy-induced hypertension-preeclampsia syndrome. *American Journal of Obstetrics and Gynecology* 1986; **154**: 792-800.
2. WEINSTEIN L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. *American Journal of Obstetrics and Gynecology* 1982; **142**: 159-67.
3. GOODLIN RC. Expanded toxemia syndrome or gestosis. *American Journal of Obstetrics and Gynecology* 1986; **154**: 1227-33.
4. MACKENNA J, DOVER NL, BRAME RG. Preeclampsia associated with hemolysis, elevated liver enzymes and low platelets—an obstetric emergency? *Obstetrics and Gynecology* 1983; **62**: 751-4.
5. PRITCHARD JA, WEISMAN R, RATNOFF OD, VOSBURGH GJ. Intravascular hemolysis, thrombocytopenia and other hematologic abnormalities associated with severe toxemia of pregnancy. *New England Journal of Medicine* 1954; **250**: 89-98.
6. MCKAY DG. Hematologic evidence of disseminated intravascular coagulation in eclampsia. *Obstetrical and Gynecological Survey* 1972; **27**: 399-417.
7. PERKINS RP. Thrombocytopenia in obstetric syndromes—a review. *Obstetrical and Gynecological Survey* 1979; **34**: 101-14.
8. AARNOUTSE JG, HOUTHOF WJ, WETTS J, VELLENGA E, HUISJES HJ. A syndrome of liver damage and intravascular coagulation in the last trimester of normotensive pregnancy. A clinical and histopathological study. *British Journal of Obstetrics and Gynaecology* 1986; **93**: 145-55.

CASE REPORT

Pneumonectomy in a patient with ventricular septal defect

R. G. MACGILLIVRAY, D. A. ROCKE, D. M. SHAMA AND A. S. MITHA

Summary

A young man with severe unilateral bronchiectasis and a ventricular septal defect presented for pneumonectomy. Intra-operative monitoring, which included continuous measurement of systemic and pulmonary oxygen saturations by oximetry, revealed transient reversal of the intracardiac shunt across the defect. The implications of this combination of cardiac and pulmonary disease for anaesthetic management are discussed.

Key words

Anaesthesia: thoracic.

Monitoring: pulse oximetry.

Pneumonectomy continues to be associated with morbidity and mortality in spite of progress in knowledge and technology in pulmonary physiology, anaesthetics and thoracic surgery. Patients with pre-existing cardiac disease may be regarded as at particular risk from peri-operative complications.

Case history

A 20-year-old male was referred to the thoracic surgical unit because of a chronic productive cough and with the chest radiograph shown in Fig. 1. He was found on admission to have a left parasternal thrill and a grade 5/6 systolic murmur, and he admitted to having defaulted from cardiology follow-up 9 years previously. Examination of the hospital records confirmed a clinical diagnosis of ventricular septal defect (VSD) originally made in association with an episode of infective endocarditis.

The duration and degree of his symptoms suggested severe bronchiectasis with minimal function of the left lung. Bronchography confirmed the presence of extensive left bronchiectasis. On pulmonary function testing, the forced expiratory volume in 1 second (FEV_1) was 2.12 litres (predicted 4.36 litres), the forced vital capacity (FVC) 3.02 litres (predicted 5.34 litres) and the FEV_1/FVC ratio 70%. These values, in conjunction with a ventilation-perfusion isotope scan which revealed neither significant ventilation nor perfusion of the left lung, suggested that left pneumonectomy was an appropriate form of treatment.

Cardiac catheterisation confirmed the presence of a small VSD with a 20–30% left-to-right shunt and minimal pulmonary hypertension (mean pulmonary artery pressure 22

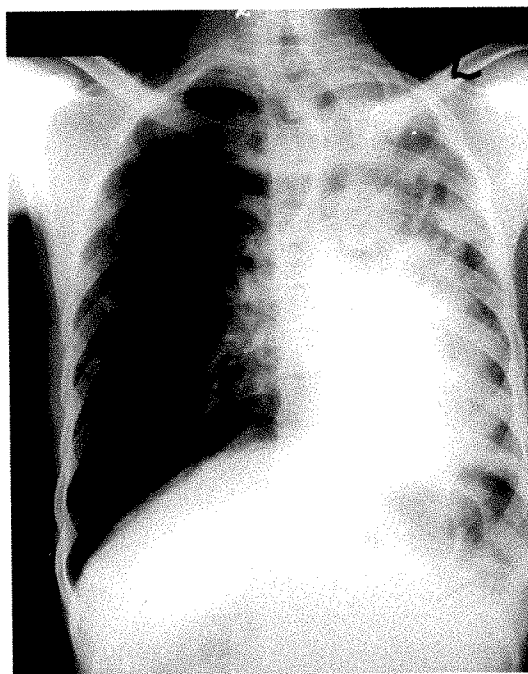


Fig. 1. Postero-anterior chest radiograph which demonstrates severely diseased left lung and mediastinal displacement.

mmHg). Balloon occlusion of the left pulmonary artery was not attempted, since no suitable catheter was available. On the day before his operation, a flow-directed oximetry catheter was introduced via the left external jugular vein and the distal end sited in the right pulmonary artery with

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fluoroscopic confirmation. Oxygen saturation was monitored continuously overnight.

Lorazepam 2.5 mg was given sublingually 2 hours pre-operatively on the morning of surgery. Electrocardiogram leads were attached and a peripheral venous cannula and radial artery cannula inserted on arrival in the operating room. Arterial oxygenation was monitored using a pulse oximeter. Baseline haemodynamic measurements were recorded, including pulmonary blood flow by thermodilution, and blood samples were drawn from the radial artery, pulmonary artery and right atrium for saturation determinations. Good correlations between direct and indirect oximetry of systemic and pulmonary arterial blood were confirmed. All measurements were repeated after the patient had breathed oxygen for 3 minutes.

Anaesthesia was induced using fentanyl 10 µg/kg and thiopentone 4 mg/kg. Suxamethonium 1 mg/kg was administered and a rigid bronchoscope inserted before introduction of a 39-FG left-sided PVC double lumen tube. Confirmation of correct tube position was obtained by fiberoptic endoscopy. Anaesthesia was maintained with halothane 1–1.5% in a 50% oxygen–nitrogen mixture. Pancuronium 0.1 mg/kg was given to provide continued muscle relaxation.

The operation proceeded without incident; ventilation to the left lung was stopped when the left pleural cavity was opened. Blood loss was minimal and pulmonary capillary wedge pressure (PCWP) and central venous pressure (CVP) were maintained within normal limits by infusion of 1000 ml Ringer lactate solution. An epidural catheter was inserted at the T₆₋₇ interspace on completion of surgery, for provision of postoperative analgesia. A rigid bronchoscope was introduced on removal of the double lumen tube to inspect the suture line and to aspirate any residual secretions. Subsequently, relaxation was reversed and the patient returned to the recovery room where he breathed spontaneously.

In the recovery area, fentanyl 100 µg in 10 ml saline was administered through the epidural catheter and resulted in good analgesia. The patient was transferred to the thoracic intensive care unit where all monitoring was continued overnight. The following morning he was well and all lines were removed. He was discharged home on the eighth post-operative day.

Haemodynamic consequences of pneumonectomy

Systemic and pulmonary arterial oxygen saturations and pressures were monitored continuously throughout the peri-operative period. In addition, blood flow was estimated by thermodilution and blood samples were obtained after induction of anaesthesia, on institution of one-lung ventilation, immediately before and after occlusion of the left main pulmonary artery, on closure of the chest, on resumption of spontaneous respiration and 1, 4 and 24 hours post-operatively in the intensive care unit.

The effects of peri-operative events on shunt flow across the VSD (\dot{Q}_p/\dot{Q}_s , see Appendix) are shown in Fig. 2 in relation to changes in mean pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR), systemic vascular resistance (SVR) and the ratio PVR/SVR; this ratio showed the closest correlation with shunt flow. Arterial blood gas values are shown in Table 1.

PAP, PVR and SVR were all elevated immediately before

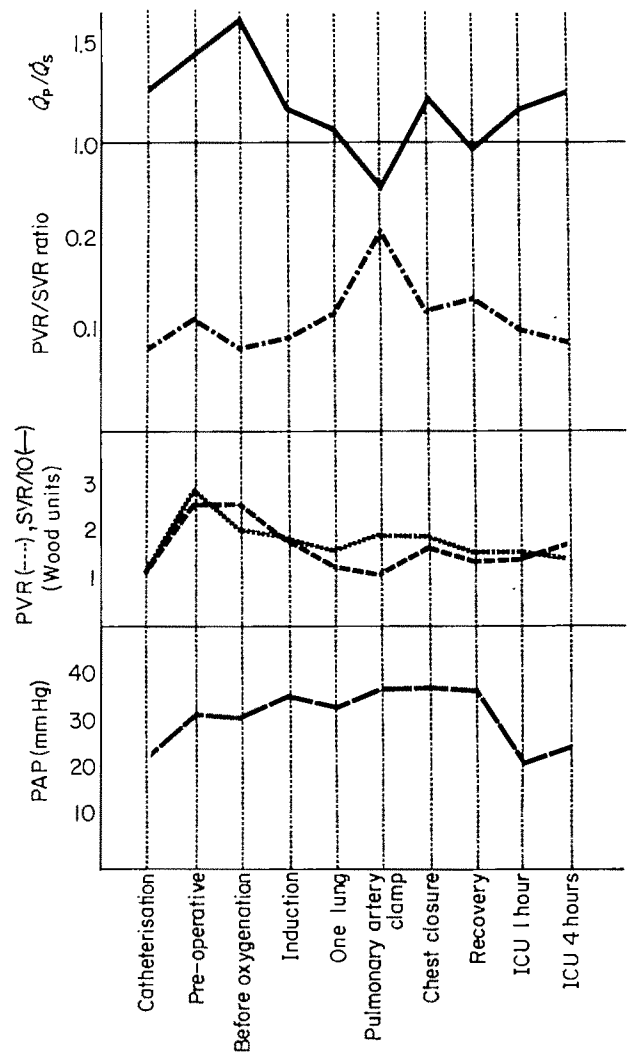


Fig. 2. Haemodynamic changes in the peri-operative period showing shunt reversal at time of pulmonary artery occlusion. \dot{Q}_p/\dot{Q}_s , Ratio of pulmonary/systemic blood flow; PVR, pulmonary vascular resistance (Wood units); SVR, systemic vascular resistance (Wood units); PAP, mean pulmonary arterial pressure (mmHg).

Table 1. Arterial oxygenation.

Time	F _{IO} ₂	P _a O ₂ (kPa)	SaO ₂ (%)
Pre-operative	0.21	10.3	95.5
Pre-oxygenation	1.0	61.7	99.9
Postinduction	0.5	17.8	98.8
One lung ventilation	0.5	12.6	96.7
After clamping	0.5	10.1	94.7
Chest closed	0.5	13.4	97.3
Bronchoscopy	1.0	45.2	99.7
ICU			
1 hour	0.4	14.5	97.5
4 hours	0.4	10.6	94.6
24 hours	0.4	11.0	95.6

operation in comparison to the values obtained in the catheterisation laboratory. Administration of 100% oxygen prior to induction of anaesthesia led to a decrease in PVR; SVR remained unchanged and, consequently, there was an increase in the shunt fraction. With induction of anaesthesia, SVR decreased to a greater extent than PVR, and shunt fraction decreased. One lung ventilation had little effect on haemodynamics since there was little perfusion of the left lung. Nevertheless, the arterial oxygen tension (P_aO₂) decreased.

Application of the left pulmonary artery clamp led to a

modest elevation in PAP (from 32 to 36 mmHg) and PVR, although the latter value was still below baseline. Since SVR remained low, the resultant change in the PVR/SVR ratio was sufficient to cause shunt reversal and a further decrease in P_{aO_2} . However, right-to-left shunting was transient and had reversed by the time the pneumonectomy was completed.

Pre-operative status was regained within one hour of return to the intensive care unit and remained unchanged for as long as the monitoring was continued.

Discussion

Extensive bronchiectasis is common in our population; the selection of such patients for surgical management was recently reviewed.¹ The obliteration of the pulmonary vascular bed by the disease process may lead to the development of pulmonary hypertension, which may constitute a contraindication to surgery.²

This patient was of particular concern, since a VSD is an additional risk factor for the development of pulmonary hypertension. The diseased lung was a source of continued infection and could have resulted in the development of further bacterial endocarditis. However, diminution of the pulmonary vascular bed by lung resection might have increased PVR sufficiently to cause shunt reversal or Eisenmenger's syndrome. The perfusion scan suggested that there was minimal blood flow to the left lung and PVR at cardiac catheterisation was low (90 dyne sec/cm²), which suggested that pneumonectomy would not result in significant haemodynamic disturbance.³

The isotope scan demonstrated almost no perfusion of the left lung but the decreased P_{aO_2} which accompanied the change to one lung ventilation, and the further decrease associated with an increase in PAP when the pulmonary artery was clamped, suggest that some blood was flowing to the left lung. Hypoxic vasoconstriction may have contributed to the minimal perfusion at scanning, and might have been inhibited during operation by a number of factors including vasoactive metabolites,⁴ endotoxins⁵ and anaesthetic agents (halothane).⁶ However, the effect of anaesthetic agents may have been overemphasised in the past by inappropriate extrapolation from animal experiments.⁷ Despite these observations, the patient did not become hypoxaemic while he received 50% oxygen.

Pulmonary arterial pressure and pulmonary and systemic vascular resistances immediately before operation were higher than the values recorded during pre-operative catheterisation and may have reflected a degree of anxiety in the patient which was not apparent clinically. Induction of anaesthesia led to a greater decrease in SVR than PVR; the latter may have been influenced by the stimulus of bronchoscopy and intubation.⁸ Pulmonary arterial pressure at the time of clamping (36 mmHg) placed the patient in a high risk category as defined by Rams *et al.*⁹ who reported a correlation between post-pneumonectomy cardio-pulmonary death and an intra-operative occlusion pressure in excess of 32 mmHg. However, that study was undertaken on patients with bronchial carcinoma in whom functioning lung was to be excised; the validity of intra-operative measurement as a predictor of postoperative status must be questioned.

We elected not to use nitrous oxide, since the presence of an intracardiac catheter together with an intracardiac

shunt increases the possibility of systemic air embolism; in addition, nitrous oxide may have a deleterious effect on PVR.¹⁰ We employed a balanced narcotic/relaxant/inhalation anaesthetic technique. The use of halothane appeared to cause little change in blood gas status when one-lung anaesthesia was used.¹¹

The use of the oximetric pulmonary artery catheter was another major departure from our normal practice. This enabled close monitoring of the patient's haemodynamic status but did not materially affect the conduct of anaesthesia or surgery. In contrast, the pulse oximeter provided useful information during one lung ventilation.

Appendix

Fick principle:

$$\dot{Q}_P = \frac{\dot{V}O_2}{C_{LAO_2} - C_{PAO_2}} \quad \text{and} \quad \dot{Q}_S = \frac{\dot{V}O_2}{C_{aO_2} - C_{\bar{v}O_2}}$$

Thus,

$$\frac{\dot{Q}_P}{\dot{Q}_S} = \frac{C_{aO_2} - C_{\bar{v}O_2}}{C_{LAO_2} - C_{PAO_2}}$$

or,

$$\frac{\dot{Q}_P}{\dot{Q}_S} = \frac{S_{aO_2} - S_{\bar{v}O_2}}{S_{aO_2} - S_{PAO_2}}$$

where \dot{Q}_P = pulmonary blood flow, \dot{Q}_S = systemic blood flow, C_{O_2} = blood oxygen content, a denotes arterial, \bar{v} mixed venous (right atrial), LA left atrial, and PA pulmonary arterial.

References

1. LE ROUX BT, MOHLALA ML, ODELL JA, WHITTON ID. Suppurative diseases of the lung and pleural space. II. Bronchiectasis. *Current Problems in Surgery* 1986; **23**: 93-159.
2. GASS GD, OLSEN GN. Preoperative pulmonary function testing to predict postoperative morbidity and mortality. *Chest* 1986; **89**: 127-35.
3. FEE HJ, HOLMES EC, GEWIRTZ HS, RAMMING KP, ALEXANDER JM. Role of pulmonary vascular resistance measurements in preoperative evaluation of candidates for pulmonary resection. *Journal of Thoracic and Cardiovascular Surgery* 1978; **75**: 519-24.
4. WEIR EK, GROVER RF. The role of endogenous prostaglandins in the pulmonary circulation. *Anesthesiology* 1978; **48**: 201-12.
5. WEIR EK, MLCZOCZ J, REEVES JT, GROVER RF. Endotoxin and prevention of hypoxic pulmonary vasoconstriction. *Journal of Laboratory and Clinical Medicine* 1976; **88**: 975-83.
6. BERTNAES LJ. Hypoxia-induced pulmonary vasoconstriction in man: inhibition due to diethyl ether and halothane anesthesia. *Acta Anaesthesiologica Scandinavica* 1978; **22**: 570-88.
7. BENUMOF JL. One-lung ventilation and hypoxic pulmonary vasoconstriction: implications for anesthetic management. *Anesthesia and Analgesia* 1985; **64**: 821-33.
8. SORESENSEN MB, JACOBSEN E. Pulmonary hemodynamics during induction of anesthesia. *Anesthesiology* 1977; **46**: 246-51.
9. RAMS JJ, HARRISON RW, FRY WA, MOULDER PV, ADAMS WE. Operative pulmonary artery pressure measurements as a guide to postoperative management and prognosis following pneumonectomy. *Diseases of the Chest* 1962; **41**: 85-90.
10. SCHULTE-SASSE U, HESS W, TARNOW J. Pulmonary vascular responses to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology* 1982; **57**: 9-13.
11. ROGERS SN, BENUMOF JL. Halothane and isoflurane do not decrease P_{aO_2} during one-lung ventilation in intravenously anesthetized patients. *Anesthesia and Analgesia* 1985; **64**: 946-54.

APPARATUS

The accuracy of pulse oximeters

A comparative clinical evaluation of five pulse oximeters

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Summary

The accuracy of five commercially available pulse oximeters was compared against arterial blood oxygen saturation, under similar clinical conditions. The oximeters had very similar performance in the clinically useful range of 80–100%, with a tendency slightly to underestimate the true saturation.

Key words

Equipment; pulse oximeters.

Pulse oximetry was first described in 1975¹ and allows the continuous non-invasive monitoring of arterial oxygen saturation. It is only recently, however, with the ready availability of various pulse oximeters from different manufacturers, that the full potential of this technology both in the peri-operative period^{2–4} and in intensive care,⁵ has been realised.

All pulse oximeters work on a similar principle, namely, absorption spectroscopy; however, considerable differences exist in the way different manufacturers obtain and process the data. These differences occur in the light-emitting diodes, sampling frequency, microprocessor algorithms and constants used in the calculations. Manufacturers' specifications of accuracy for pulse oximeters are all similar in the clinically useful range (± 1 –2%) and, in some cases, papers have been published to support this.^{6–8} These results were often obtained in highly controlled, non-clinical situations. The purpose of this study was to compare simultaneously the accuracy of various pulse oximeters available at the time of the study, in patients undergoing surgery or in intensive care.

Methods

Patients who had arterial lines in position as part of their management in the operating theatre or intensive care unit were studied; most of the data were obtained from patients in intensive care. The lungs of some of the patients were artificially ventilated; some were being weaned from mechanical ventilation and others breathed spontaneously.

The five pulse oximeters used were the Biox 3700 (Ohmeda), Nellcor N100 (Draeger), Bird 4400 (MIE), Criticare 501 (Simonsen & Weel) and Novometrix 500

(Vickers). Their specifications are outlined in Table 1. Each of these oximeters has a choice of probes, for example for finger or earlobe, but only the finger probes were used in order to limit variation. Some of the instruction manuals suggest the index and middle fingers are the preferred sites for the finger probes. This enabled us to test four oximeters at any one time, two probes on each hand. However, this means that the data are not strictly comparable in terms of the recording site for every saturation reading and every machine. One machine, the Biox 3700, was used throughout to provide a standard for comparison.

It was determined prior to the start of the study that no interference was caused by placing probes on adjacent fingers. User-related error is small with pulse oximeters because no user calibration is required and the machines perform an internal system and calibration check each time they are switched on. Little variation is possible in response to the correct placement of finger probes. The oximeters were all used in their standard averaging-time mode for the calculation of saturation.

Saturation readings were recorded only when each machine indicated a good perfusion signal, the reading was stable and no other malfunction warning displayed. A heparinised arterial blood sample was withdrawn from the indwelling arterial line at the same time as the oximeter readings were recorded. The blood samples were stored in crushed ice and analysed within one hour on a calibrated IL282 co-oximeter. The calibration was performed to manufacturer's specification⁹ before and after each batch of samples was analysed.

Statistical analysis of the data was by least-squares linear regression analysis and calculation of correlation coefficients.

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Table 1. Specifications of pulse oximeters evaluated.

	Bird 4400	Criticare 501	Novometrix 500	Biox 3700	Nellcor N100
Weight (kg)	0.9	0.8	4.36	4.11	7.0
Dimensions (mm)					
Depth	190	190	256	286	295
Width	139	139	230	250	305
Height	68	45	91	90	100
Battery life (hours)	18*	12	10	1.5	1
Display	Sao ₂ † Pulse rate	Sao ₂ † Pulse rate	Sao ₂ Pulse rate amplitude Alarm settings	Sao ₂ Pulse rate amplitude Plethysmograph Alarm settings	Sao ₂ Pulse rate amplitude
Sao ₂ trend and memory	—	—	—	20- and 60-minute trend; 8-hour memory Sao ₂	—
Averaging time settings	Fixed	Fixed	2, 4, 8, 16 seconds	3, 6 seconds	5-7, 2-3, 10-15 seconds
Outputs	Analogue, RS232c	Analogue, RS232c	Analogue	Analogue, RS232	Fibreoptic interface
Probes					
Adult	Finger, multisite	Finger, multisite	Finger, ear	Finger, ear	Finger, nasal‡
Paediatric	Multisite	Multisite	2‡	2	3‡

* Non-illuminated display.
† No pulse rate or high saturation alarms.
‡ Limited probe life.

Table 2. Results.

	Regression equation	Correlation coefficient	Values underestimating IL282 saturation (%)	Mean value of underestimate (%)
Bird 4400	$y = 1.23x - 24.4$	0.981	93	2.34
Criticare 501	$y = 1.11x - 11.7$	0.966	85	2.0
Novometrix 500	$y = 0.734x + 23.3$	0.878	83	2.8
Biox 3700	$y = 1.06x - 7.71$	0.976	87	2.4
Nellcor N100	$y = 1.1x - 11.4$	0.979	82	2.0

Results

Data were obtained from 20 patients and between 70 and 100 readings were made on each machine. No results were included from any patient who was jaundiced or had carboxyhaemoglobin and methaemoglobin levels that totalled greater than 3.5% (as a result of analysis on the IL282 co-oximeter). This minimises errors from these sources which can cause differences in saturation readings obtained by pulse oximeter and co-oximeter analysis.²

Table 2 gives the regression equations that express each oximeter's saturation readings as a linear function of the IL282-determined saturations, together with correlation coefficients. The results are plotted and regression lines drawn in Figs 1-5.

With no oximeter was there a normal distribution of saturation readings around the IL282-determined values. There was a tendency in all machines consistently to underestimate the true saturation values in the 80-100% range, where most of the readings in this study were obtained. Thus between 82-93% of readings were underestimates and the mean value of this error varied between 2.0% and 2.8%, depending on the oximeter used (Table 2).

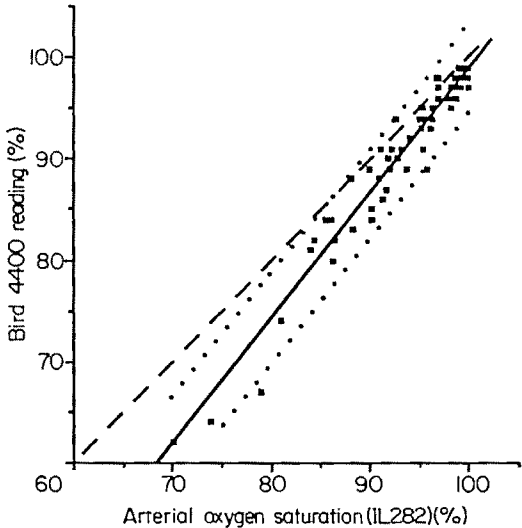


Fig. 1. Relation between oximeter reading and saturation measured in arterial blood samples by IL282 co-oximeter analysis for Bird 4400. —, Regression line; ---, line of identity; ····, 95% confidence limits.

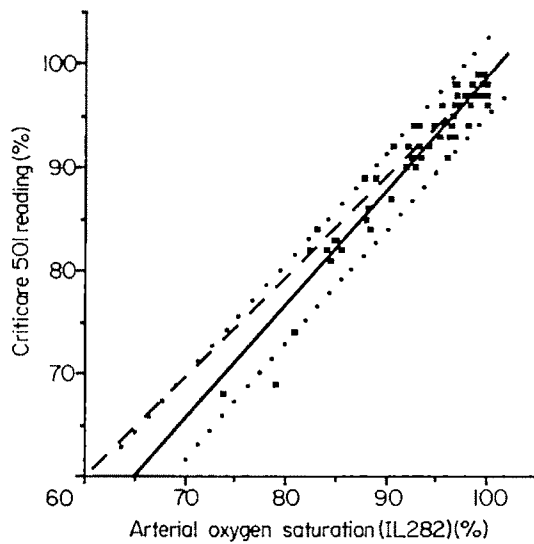


Fig. 2. Relation between oximeter reading and saturation measured in arterial blood samples by IL282 co-oximeter analysis for Criticare 501. —, Regression line; --, line of identity; ·····, 95% confidence limits.

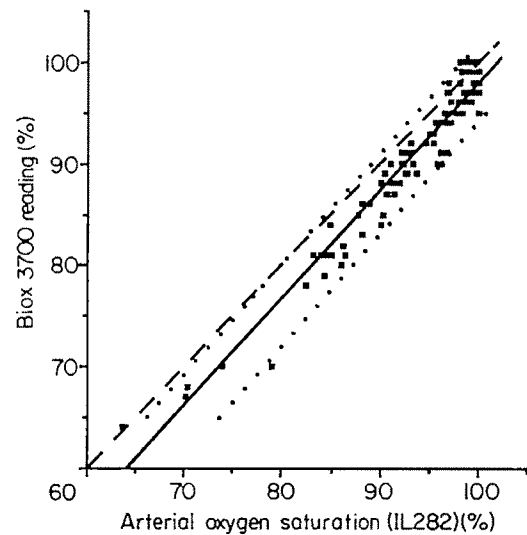


Fig. 4. Relation between oximeter reading and saturation measured in arterial blood samples by IL282 co-oximeter analysis for Biox 3700. —, Regression line; --, line of identity; ·····, 95% confidence limits.

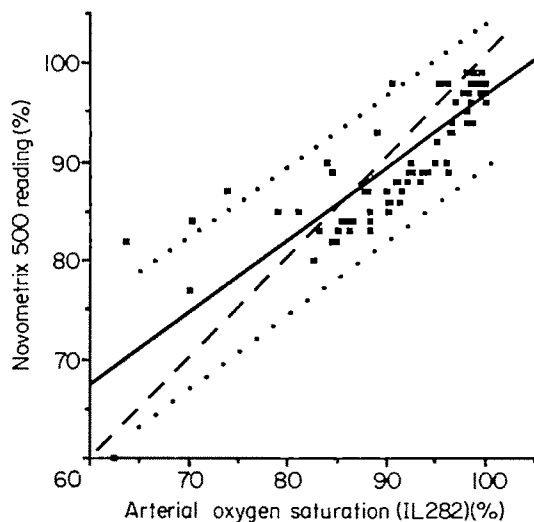


Fig. 3. Relation between oximeter reading and saturation measured in arterial blood samples by IL282 co-oximeter analysis for Novomatrix 500. —, Regression line; --, line of identity; ·····, 95% confidence limits.

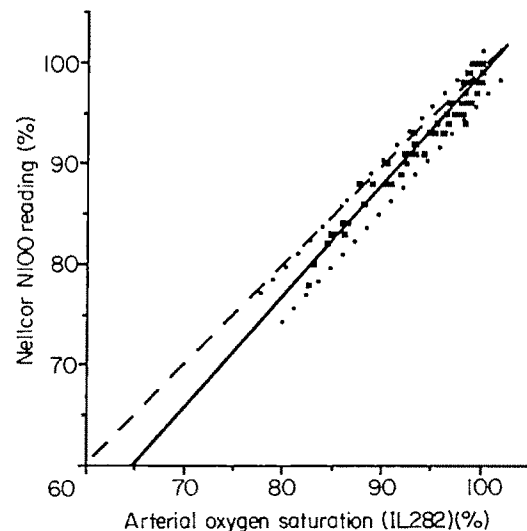


Fig. 5. Relation between oximeter reading and saturation measured in arterial blood samples by IL282 co-oximeter analysis for Nellcor N100. —, Regression line; --, line of identity; ·····, 95% confidence limits.

Discussion

The cutaneous determination of arterial oxygen saturation was first investigated over 40 years ago¹⁰ but, despite much refinement of the method, it never became a straightforward, accurate procedure suitable for routine continuous clinical use. The advent of pulse oximetry has made this possible and many departments are now acquiring this equipment.

The principles upon which pulse oximeters function are relatively simple but, in practice, there are probably more variables and potential sources of error than occur in the determination of many other physiological variables. These variations result from differences in light-emitting diodes and their outputs, in the sampling frequency of the diodes, in the algorithms used in the calculations and in the number of calculations per second. The constants and correction

factors used in the algorithms also vary and these depend, in part, on the population type and size used in their initial determination.

The results of this study show that, under similar conditions of evaluation, most of the pulse oximeters gave a similar degree of accuracy and, in general, tended slightly to underestimate the arterial oxygen saturation. This is undoubtedly safer in clinical practice than, for example, persistent overestimation of saturation, or large unpredictable variations. One of the pulse oximeters did have a larger variation of saturation than the other machines and this appeared to be related to the positioning of the finger probe, which has been modified on later versions of this machine. These results do not mean that pulse oximeters will perform identically under adverse conditions such as low perfusion states or at very low saturation levels, where the error in determined saturation was shown to be large

with a now superseded pulse oximeter.¹¹ All pulse oximeters should detect satisfactorily changes and trends in arterial saturation which are very important during both anaesthesia and recovery and in intensive care. It is likely on the standard averaging-time setting (i.e. 4–6 seconds), that there is little difference in the accuracy of trend-following ability between the various machines, because any advantages of more frequent data sampling or algorithm calculations are largely lost in the averaging.

All these machines provide an alarm in response to the precritical incident of a rapid decrease in arterial oxygen saturation. Only those with a memory or trend display will pre-empt a potentially serious deterioration in a patient before the critical alarm level is reached.

If all pulse oximeters are of approximately equal accuracy in normal usage, then equipment can be chosen on the basis of considerations such as those listed in Table 3. The

Table 3. Features to consider in selection of a pulse oximeter.

Accuracy

Proposed usage

Continuous monitoring in theatre

Backlight illumination essential

Direct mains electricity versus external charger

Suitability and range of probes (e.g. ear, paediatric)

Alarms: high/low, adjustable, settings

Memory

Plethysmographic display

Transport of patients

Battery life

Size, weight, portability

Recovery use

Ease of use

Will probe stay on an awake patient?

Alarms and false alarm discrimination

Patient assessment, ITU, research

Internal data storage

Interface with printers, computers, etc.

Capital outlay and running costs

Probe replacement, maintenance

machines evaluated in this study vary considerably in their suitability for the various possible uses (Table 1). The Biox 3700 differs from the other machines in that it displays the plethysmographic arterial waveform. This allows the user a subjective assessment of the quality of the signal that is processed and, to some extent, of the shape of the arterial pulse wave. It does not function, however, as a quantitative digital plethysmograph, because the gain of the signal is automatically adjusted to fill the display screen.

In conclusion, the accuracy of the pulse oximeters evaluated in this study was similar in the 80–100% arterial oxygen saturation range, with a consistent tendency slightly to underestimate the true saturation. Careful consideration of usage, for example continuous monitoring in the operating theatre, during recovery from anaesthesia, during patient transport or for research in intensive care, must be made before a particular pulse oximeter is acquired, because specification differences between the large number now

available make some machines more suitable than others for any particular use. Machines with a pulse wave display and a prolonged memory and trend facility for oxygen saturation (e.g. the Biox 3700 in this group of instruments), have a greater versatility and wider application which give them an advantage over machines without these features.

Addendum

Following the submission of this paper, two other studies that evaluated pulse oximeter accuracy in normal volunteers have become available. One study¹² evaluated the Biox 3700 and found the finger probe (but not the ear probe) significantly to underestimate arterial saturation, and the manufacturers modified the software to correct this error. This study also showed that pulse oximetry of the ear detected changes in arterial saturation more rapidly than the finger. This is a physiological phenomenon and not due to the pulse oximeter.

Another study¹³ evaluated the accuracy of pulse oximeters at very low saturation levels (40–70%). This found, like the present study, that the Novometrix 500 varied greatly in accuracy. The manufacturers made modifications as a result and repeat observations showed great improvement, at least in the low saturation range studied.

References

1. NAKAJIMI S, HIRAI Y, TAKASE H, KUSE A. New pulse-type earpiece oximeter. *Respiration and Circulation* 1975; **23**: 709–13.
2. TAYLOR MB, WHITWAM JG. The current status of pulse oximetry. Clinical value of continuous noninvasive oxygen saturation monitoring. *Anaesthesia* 1986; **41**: 943–9.
3. BRODSKY JB, SHULMAN MS, SWAN M, MARK JBD. Pulse oximetry during one-lung ventilation. *Anesthesiology* 1985; **63**: 212–4.
4. MOTOYAMA EK, GLAZENER CH. Hypoxemia after general anesthesia in children. *Anesthesia and Analgesia* 1986; **65**: 267–72.
5. CECIL WT, PETTERSON MT, LAMOONPUN S, RUDOLPH CD. Clinical evaluation of the Biox MIA ear oximeter in the critical care environment. *Respiratory Care* 1985; **30**: 179–83.
6. SARNQUIST FH, TODD C, WHITCHER C. Accuracy of a new non-invasive oxygen saturation monitor. *Anesthesiology* 1980; **53**: S163.
7. YELDERMAN M, NEW W. Evaluation of pulse oximetry. *Anesthesiology* 1983; **59**: 349–52.
8. REBUCK AS, CHAPMAN KR, D'URZO A. The accuracy and response characteristics of a simplified ear oximeter. *Chest* 1983; **83**: 860–4.
9. *Operator's manual, IL282 co-oximeter*. Lexington, MA: Instrumentation Laboratory Inc., 1980.
10. SQUIRE JR. An instrument for measuring the quantity of blood and its degree of oxygenation in the web of the hand. *Clinical Science* 1940; **4**: 331–7.
11. CHAPMAN KR, LIU FL, WATSON RM, REDBUCK AS. Range of accuracy of two wavelength oximetry. *Chest* 1986; **89**: 540–2.
12. KAGLE DM, ALEXANDER CM, BERKO RS, GIUFFRÉ M, GROSS JB. Evaluation of the Ohmeda 3700 pulse oximeter: steady-state and transient response characteristics. *Anesthesiology* 1987; **66**: 376–80.
13. SEVERINGHAUS JW, NAIFEH KH. Accuracy of response of six pulse oximeters to profound hypoxia. *Journal of Clinical Monitoring* 1987; (in press).

APPARATUS

Measurement of FEV₁ and FVC

Comparison of a pocket spirometer with the Vitalograph

H. E. HOSIE AND W. S. NIMMO

Summary

The performance of a pocket spirometer was compared with that of the Vitalograph to assess the extent of agreement between the instruments and the repeatability of measurements with each instrument. Both instruments showed a similar level of accuracy when measurements were repeated and in the estimation of forced vital capacity, but there was a mean difference of 201 ml in measurements of forced expiratory volume in one second, for which the Vitalograph gave the larger reading.

Key words

Measurement techniques; spirometry.

The Vitalograph is the standard instrument used to measure the forced expiratory volume in one second (FEV₁) and the forced vital capacity (FVC). A pocket spirometer (Micro Medical Instruments Ltd) which measures FEV₁ and FVC as well as peak expiratory flow rate, is more portable and convenient to use. The Vitalograph is operated by the patient inflating a bellows to displace a marking pen vertically on a chart which is moved horizontally at a constant speed by a motor. The pocket spirometer works on the rotating vane principle and the number of rotations is detected by an optical system. It is considerably cheaper than the Vitalograph and does not need electrical mains supply, pressure-sensitive graph paper or technical skill in interpretation of the data, since a digital display is provided.

There would be major advantages in the use of such an instrument if the estimates obtained were accurate and repeatable. We compared measurements obtained from the pocket spirometer with those from the Vitalograph.

Methods

One hundred and twenty healthy volunteers aged 4–45 years, height 1.12–1.98 m and weight 19–98 kg, took part in the study. None of the volunteers had a history of respiratory disease. Subjects were instructed to make a maximal inspiratory effort to fill their lungs, and to exhale through the mouthpiece as forcibly and as rapidly as possible. Two measurements were taken using the Vitalograph and two using the pocket spirometer, in random order. No practice was allowed but readings which were

obviously inaccurate due to faulty technique or lack of an airtight seal were ignored and the measurement repeated.

Analysis of data

Correlation coefficient. Scatter diagrams were plotted in order to examine the relationship between the two instruments. These displayed the mean of the measurements obtained using the pocket spirometer against the mean of the measurements from the Vitalograph for both FEV₁ and FVC. The correlation coefficient (*r*) was calculated for each set of data.

Agreement.¹ The difference between the first readings from each device was plotted against the average of the two readings in order to assess the extent of agreement between the instruments. This was done for both FEV₁ and FVC.

The mean of the differences between the values obtained using both instruments is known as the bias. The consistency of the bias is calculated from the mean difference and the standard deviation; the upper limit of agreement is the mean plus two standard deviations and the lower limit of agreement is the mean difference minus two standard deviations.

Any difference (or bias) in the values obtained using different instruments can be seen from these calculations and, provided that the limits of agreement are small, a consistent bias can be taken into account in the interpretation of the results.

Repeatability.¹ The average of the two readings using the same machine was plotted against the difference

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between the readings in order to assess the repeatability of measurements. The mean of the differences between the first and second readings would be expected to be zero in an instrument of high repeatability. The repeatability coefficient is expressed by calculating twice the standard deviation of the mean of the differences and is a measure of the variability between readings using the same machine.

Results

Correlation coefficient

The data points in Figs 1 and 2 are clustered around the line of equality and the high coefficients of correlation ($r = 0.9491$ for FEV_1 , 95% confidence limits 0.9127–0.9855; $r = 0.981$ for FVC, 95% confidence limits 0.956–1.005; $p < 0.001$) suggest that measurements obtained using the Vitalograph and the pocket spirometer are closely related.

Agreement

There was some disparity in the measurements between the instruments, with differences of up to 960 ml in FEV_1 and 740 ml in FVC. The magnitude of the difference was not proportional to lung volume for either FEV_1 ($r = 0.1932$) or FVC ($r = 0.0174$).

Figures 3 and 4 show similar degrees of scatter but the bias was different. The Vitalograph gave a reading for FEV_1 which was, on average, 201 ml greater than that indicated by the pocket spirometer. The bias in the FVC measurements was much less; the pocket spirometer tended to read greater by only 47 ml on average.

The limits of agreement between the Vitalograph and the pocket spirometer were wide. This suggests that the bias between the instruments is not consistent and that they probably cannot be used interchangeably. Ninety-five percent confidence limits can be calculated according to the method described by Bland and Altman¹ both for bias and for limits of agreement. Calculation of 95% confidence limits for bias in the FEV_1 measurements gives bias values

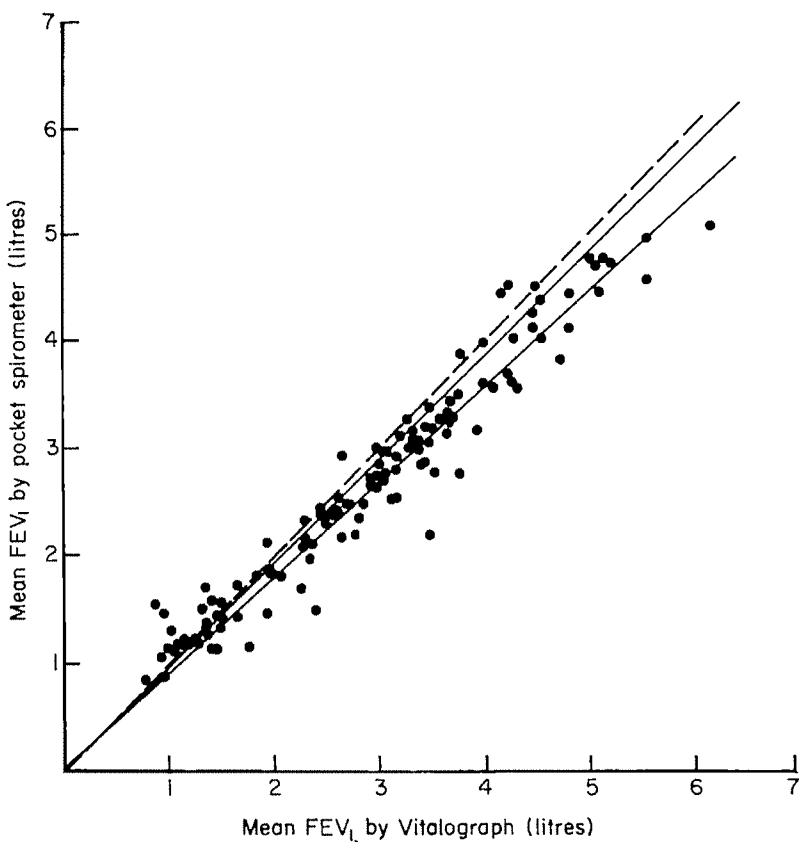


Fig. 1. FEV_1 measured using Vitalograph and pocket spirometer, with line of equality (—) and 95% confidence intervals (---). $r = 0.9491$.

Table 1. Bias, with 95% confidence intervals and limits of agreement, and repeatability coefficients when comparing measurements of FEV_1 and FVC using the Vitalograph and pocket spirometer.

	Bias (ml)	95% Confidence intervals (ml)	Limits of agreement (ml)	Repeatability coefficient	
				Spirometer	Vitalograph
FEV_1	201	151 to 250	747 to -345	376	388
FVC	-47	-6 to -87	405 to -499	354	364

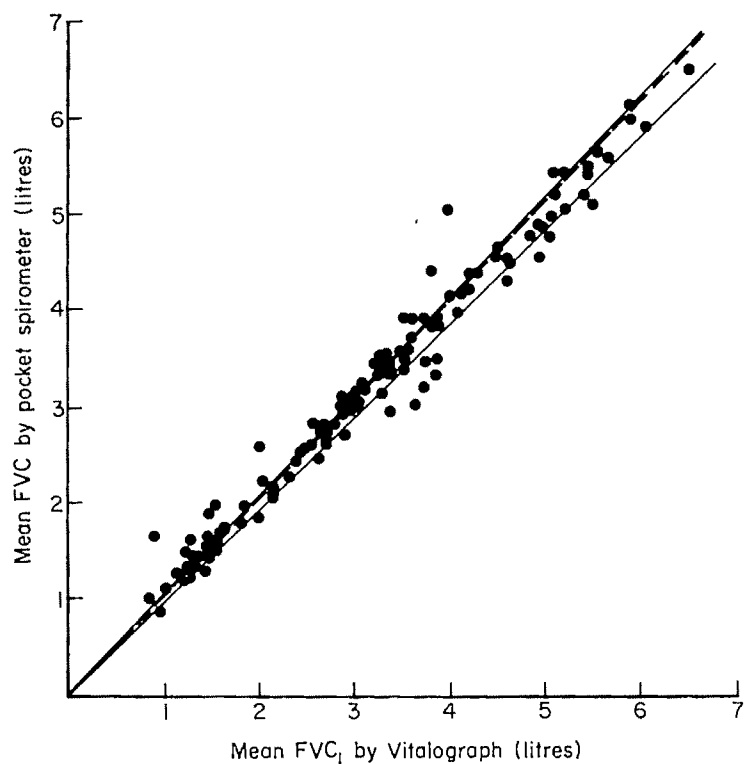


Fig. 2. FVC measured using Vitalograph and pocket spirometer, with line of equality (----) and 95% confidence intervals (—). $r = 0.981$.

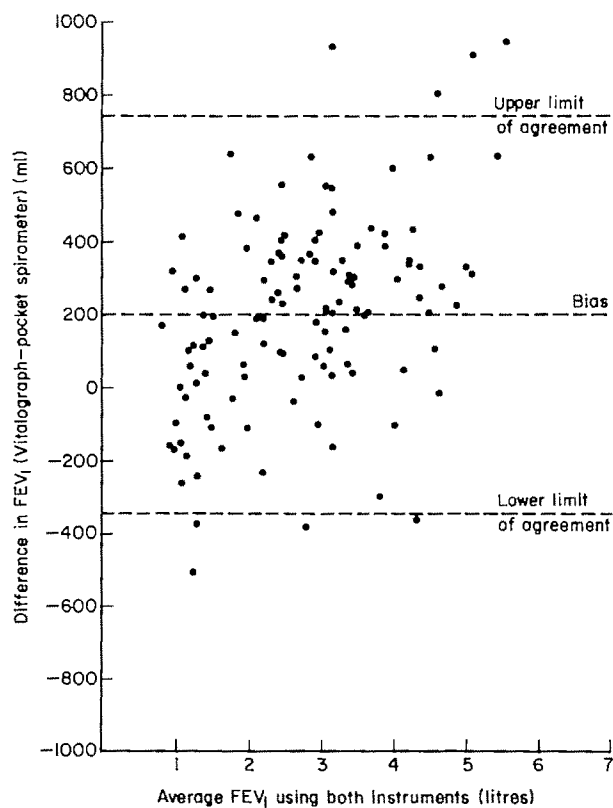


Fig. 3. Difference against the mean for FEV₁ using both instruments, with bias and limits of agreement.

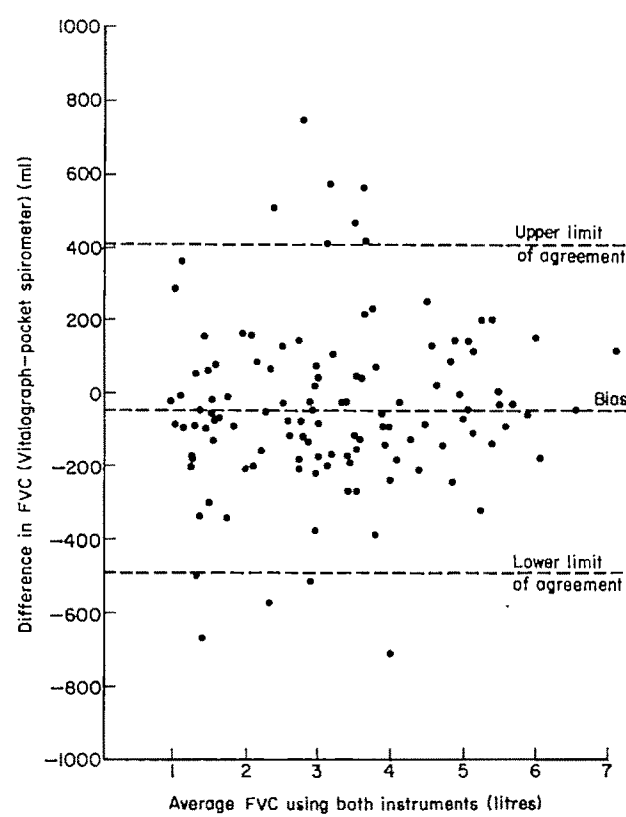


Fig. 4. Difference against the mean for FVC using both instruments, with bias and limits of agreement.

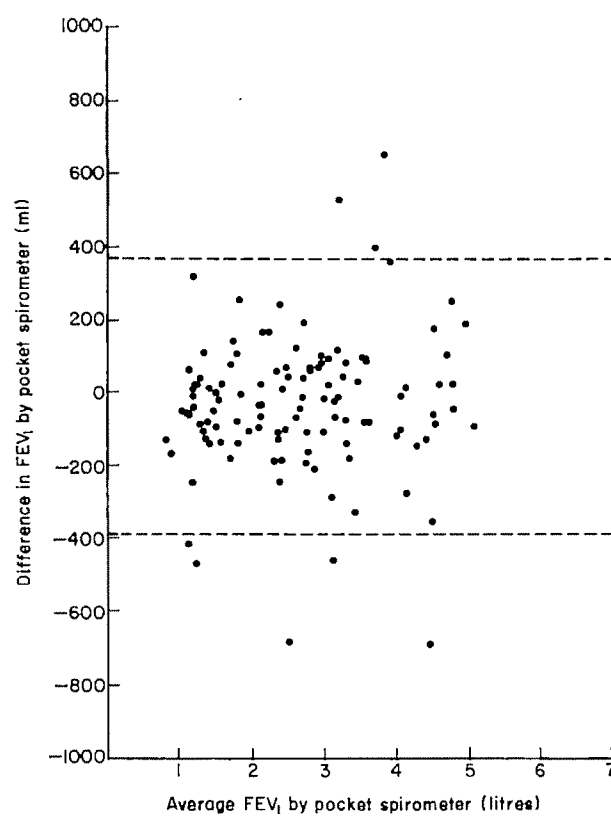


Fig. 5. Repeated measurements of FEV₁ using pocket spirometer, with repeatability coefficients (----).

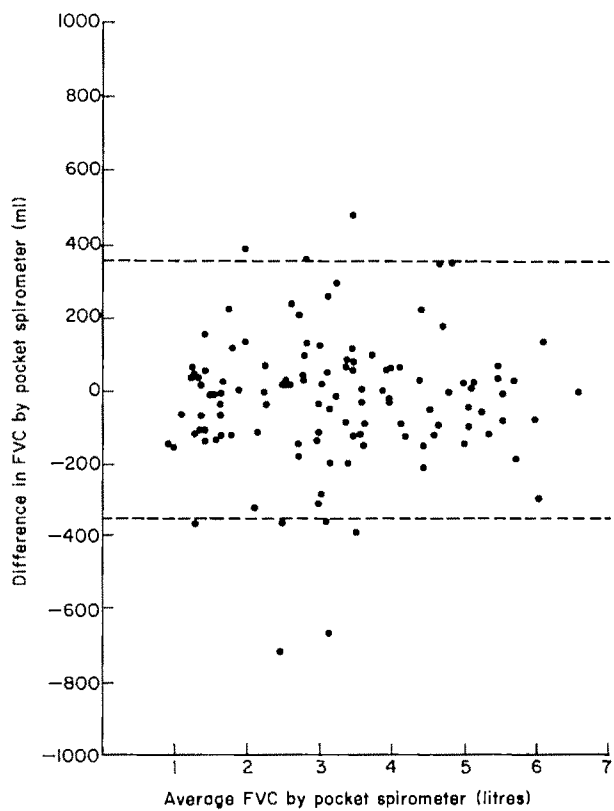


Fig. 6. Repeated measurements of FVC using pocket spirometer, with repeatability coefficients (----).

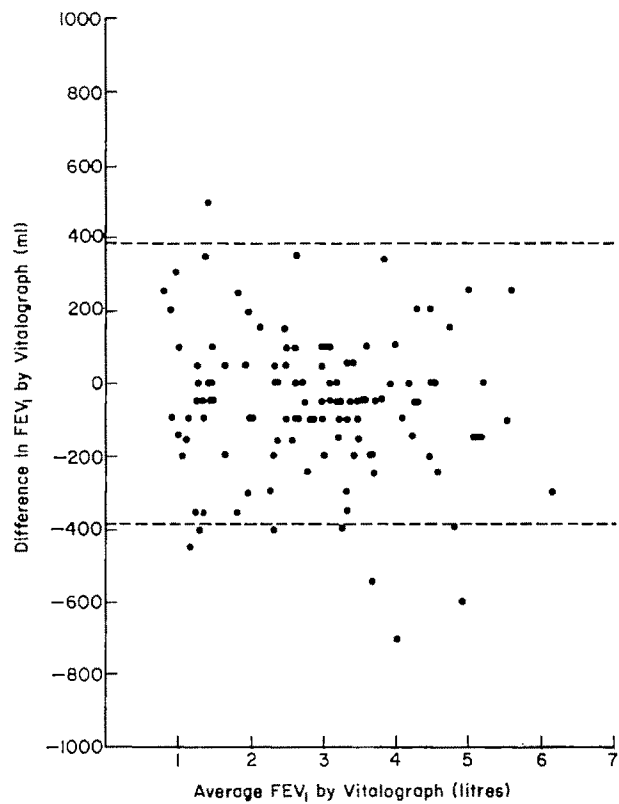


Fig. 7. Repeated measurements of FEV_1 using Vitalograph, with repeatability coefficients (----).

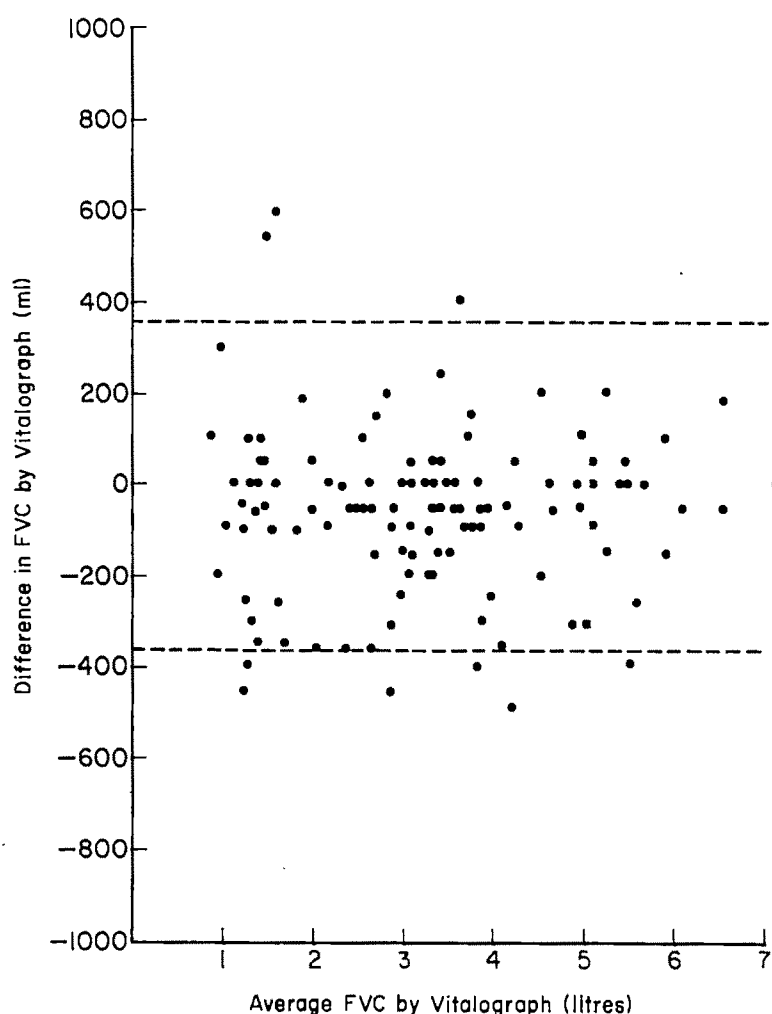


Fig. 8. Repeated measurements of FVC using Vitalograph, with repeatability coefficients (---).

that range from 150–250 ml, and the Vitalograph gives the larger reading.

Repeatability

Repeatability measurements using the pocket spirometer are shown in Figs 5 (FEV_1) and 6 (FVC) and using the Vitalograph in Figs 7 (FEV_1) and 8 (FVC). A similar range of differences is found in all four figures, with values that differ by up to 800 ml. The differences for the Vitalograph appear to be more uniform because measurements were made to the nearest 50 ml only. The mean differences were small for both instruments (–32 to –37 ml for the pocket spirometer, –61 to –63 ml for the Vitalograph) and the coefficients of repeatability were similar for both measurements (Table 1).

Discussion

The Vitalograph and the pocket spirometer are not interchangeable when measuring FEV_1 (Fig. 3). A bias of some 200 ml can be expected but this may not be an accurate estimate at low lung volumes or in the interpretation of results in patients with obstructive airways disease. The reason for this discrepancy may be related to the different

methods by which the forced expiration is timed; the pocket spirometer uses an electronic sensing system to detect the number of revolutions of a rotating vane in one second, whereas the Vitalograph depends upon a chart that moves horizontally at a constant speed.

The repeatability of the observations did not differ significantly between the two instruments but the limits of agreement and the repeatability coefficients may reflect the variability in effort by the subjects on repeated testing.

The pocket spirometer may prove to be a useful instrument in clinical practice. However, care must be taken in the interpretation of FEV_1 measurements and results using the spirometer should not be compared directly with those obtained from the Vitalograph.

Acknowledgments

We thank the Brownies of the 37th Sheffield, Ranmoor and the Guides of the 52nd Ranmoor, St John's for their assistance in providing subjects with small lung volumes.

Reference

1. BLAND JM, ALTMAN DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307–10.

Forum

The antiemetic action of propofol

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Summary

Eighty patients who underwent minor gynaecological surgery were anaesthetised with either incremental propofol or incremental methohexitone after an opioid premedication. The group anaesthetised with propofol had significantly fewer emetic sequelae and the results suggest that propofol has a definite antiemetic action.

Key words

Anaesthetics, intravenous; methohexitone, propofol. Vomiting; antiemetic.

Postoperative nausea and vomiting is an unpleasant and distressing event for many people. Early studies with the new anaesthetic induction agent propofol (Diprivan) gave the impression that the frequency of postoperative emetic symptoms was lower than after a standard barbiturate induction.^{1,2} This paper reports a study undertaken to confirm or refute this view.

Postoperative emetic symptoms are influenced by many factors such as the patient's age and sex, the nature and duration of operation and the type of anaesthesia. Prime among these is the pre- or intra-operative use of opioid analgesics. These variables were all standardised as far as possible under routine clinical conditions and the incidence of emetic sequelae following propofol anaesthesia was compared with that after methohexitone, an established barbiturate anaesthetic agent.

Patients and methods

Eighty healthy women scheduled to undergo minor gynaecological operations, but excluding termination of pregnancy, were randomly allocated to one of two premedicant groups, to receive morphine 7.5 mg or pethidine 75 mg given intramuscularly without atropine, 60–120 minutes before operation. In random order, half of the patients in each group (n = 20) were anaesthetised with propofol 2.25 mg/kg with 67% nitrous oxide in oxygen; in the remainder, propofol was replaced by the barbiturate methohexitone 1.6 mg/kg. No volatile agents were used and anaesthesia was maintained by administration of 10-mg increments of the induction agent as indicated clinically. No other drugs were given.

The patients, isolated in separate cubicles, were visited before operation and at 1 and 6 hours after operation by an anaesthetist who was unaware of the agents used. They were questioned about a range of postoperative symptoms including nausea and vomiting. For statistical purposes nausea and vomiting were combined as total emetic symptoms and the differences between the groups calculated using Chi-squared and Fisher's exact probability tests.

Results

Patients in the four series were broadly comparable with respect to mean age, weight and duration of anaesthesia (Table 1). There was a lower incidence of emetic sequelae when propofol was the anaesthetic agent (Table 2). The difference at both time intervals was statistically significant ($\chi^2 = 8.4$ – 8.6 , $p < 0.005$).

Table 1. Mean (SEM) patient age, weight and duration of surgery.

	Propofol	Methohexitone
<i>Morphine premedication</i>		
Age, years	32 (2.3)	34 (2.8)
Weight, kg	58 (5.0)	60 (4.7)
Duration, minutes	7.7 (1.38)	7.4 (0.92)
<i>Pethidine premedication</i>		
Age, years	37 (2.5)	31 (2.0)
Weight, kg	65 (2.1)	65 (5.2)
Duration, minutes	7.8 (1.27)	6.9 (0.98)

Table 2. Number of patients with postoperative emetic symptoms (n = 20 in each group).

	0–1 hour		1–6 hours	
Premedication	Methohexitone	Propofol	Methohexitone	Propofol
Morphine	8	0	13	5
Pethidine	4	2	5	1
Total	12	2	18	6
	p < 0.005		p < 0.005	

Of six patients in the methohexitone group who were nauseated prior to operation, four were still affected in the first postoperative hour. The comparable figures for propofol were seven pre-operatively and none postoperatively,

a significant difference ($p = 0.04$). This difference had disappeared by 6 hours postoperatively, at which time two patients were nauseated in each anaesthetic group (Table 3). Nausea developed in the late postoperative period in

Table 3. Outcome of patients nauseated prior to operation.

	Pre-operative	0-1 hour	1-6 hours
Propofol	7	0	2
Methohexitone	6	4	2
	$p = 0.04$		NS

five patients in the propofol series premedicated with morphine who were initially asymptomatic. This was not seen in the group given the shorter-acting agent pethidine.

Discussion

Propofol significantly reduced the emetic sequelae associated with opioid premedication under the conditions of this study. This effect appears to be of short duration, since

emetic symptoms returned in some patients premedicated with the longer-acting morphine, but is still likely to be of major benefit to patients who undergo minor or outpatient procedures.

Acknowledgments

We thank ICI plc Pharmaceuticals Division, for the supplies of propofol.

References

1. DUNDEE JW, HASLETT WHK, KELTY SR, PANDIT SK. Studies of drugs given before anaesthesia. XX. Diazepam-containing mixtures. *British Journal of Anaesthesia* 1970; **42**: 143-50.
2. STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 152-6.

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An additional tactile test

Further developments in tactile tests to confirm laryngeal placement of tracheal tubes

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Summary

An additional clinical test to confirm laryngeal placement of tracheal tubes is described. Using the new test, placement was confirmed in all of 50 patients studied in whom difficulty would have been anticipated using previously described tactile tests (male patients with lower molar teeth). Two anaesthetists with small hands averaged 98% confirmations in two series each of 100 consecutive unselected intubations. A simple modification of the tests enables their application after nasotracheal intubation; even with small hands, a confirmation rate of 96% in 50 consecutive cases was found. The three tactile tests are reviewed and analysed. In the authors' combined experience of 14 cases of difficult laryngoscopy the tests gave reliable confirmation in 12 patients. Familiarity with these tests is stressed to be important for their reliable implementation.

Key words

Intubation, tracheal.

Other tests need to be used to confirm correct placement of the tracheal tube when direct visualisation of the larynx at intubation is impossible. Almost all the clinical tests in use are indirect and their reliability has been questioned.¹

A recent paper described two complementary direct tests, based on the sense of touch, either of which allowed positive confirmation of correct placement.² However, these tests were difficult to perform in males with 'dental block' (the presence of any or all of the left lower molar teeth). A third test was devised, called the mid test, in an attempt to overcome the block produced by the molars when the side test was used.

The present study compares all three tests in 50 consecutive male patients who required tracheal intubation and who

had dental block. In addition, since the original report did not investigate the use of the tactile tests by anaesthetists with small hands, the tests were used by each of the two authors with small hands in a further group of patients. Finally, modifications to the mid and side tests were devised and then tested in 50 consecutive patients who had undergone nasotracheal intubation.

Methods

A number of the preliminary points described for the previous tests remain applicable. The tests are performed after the tracheal tube has been introduced, but before it has been tied in place. Pre-operative assessment should have

identified loose or sharp teeth. A thin disposable polythene glove is worn on the hand that enters the patient's mouth. Tooth guards were considered unnecessary in the earlier report but it is now recommended that some form of tooth guard should be used when very sharp teeth are present or when more difficult patients are tested (e.g. males with a full set of teeth). Thin polythene gloves can be torn easily by sharp teeth, particularly if insufficient care is exercised when the examining fingers are advanced into the pharynx. The area just beyond the base of the index finger on the dorsal surface of the hand is most at risk. In the case of the mid test, the tooth guard is placed over the upper left premolars; for the side test and central test,² the respective positions are over the upper left molars and over the upper incisors.

The optimum height for the patient's head is just below the level of the examiner's umbilicus. The tests are described for a right-handed examiner standing at the patient's left side.

Test 3 (mid test). Instead of extending the neck as for the mid and central tests, the head is flexed moderately and rotated through about 60° relative to the longitudinal axis so that the lower jaw lies immediately anterior to the middle of the patient's left clavicle (Fig. 1). The examiner stands



Fig. 1. The patient has been placed in position for the test. After flexion and lateral rotation of the neck, the chin has come to lie in front of the left clavicle. The tracheal tube is not tied in because this allows greater mobility of the structures while the test is performed.

on the left side of the patient, level with the lower chest.

The right index finger is introduced into the mouth to lie between the inner aspect of the patient's left lower teeth and the outer border of the tongue.



Fig. 2. The examiner's (gloved) right index finger is inserted into the mouth to lie between the inner aspect of the patient's left lower teeth and the outer border of the tongue.

the index finger stays between the tongue and the left lower teeth. Movement of the finger toward the pharynx is accompanied by an intermittent flexing of its tip to draw the tongue forward. To hook the finger round the tracheal tube (Fig. 3), further flexing of its tip draws both the tracheal

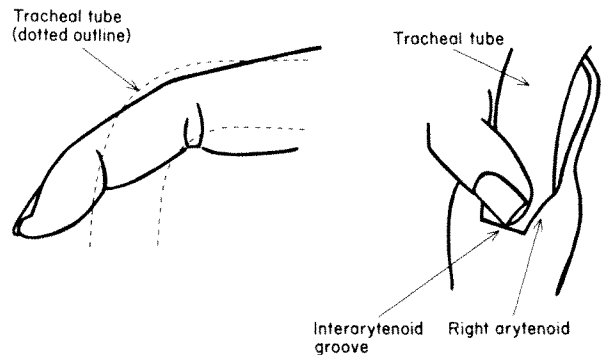


Fig. 3. The bulk of the tongue lies between the index finger and the tracheal tube, but the aim is to reach around the tongue (by drawing it forward) until the posterior surface of the tube is found. *Left*, relationship between the index finger and the tracheal tube (dotted outline). Note that, in effect, this relationship allows the finger to cut across the pathway taken by the tracheal tube. *Right*, the finger has progressed down to the interarytenoid groove. Before this can happen, the larynx needs to be moved into position (see Figs 4 and 5).

tube and tongue forward. During these manoeuvres, the edge of the epiglottis may be felt in front of the tracheal tube, although this is unusual as it tends to be covered by the tongue when the tracheal tube is pulled forward.

With the tip of the index finger hooked around the back of the tracheal tube, the thumb and index finger of the left hand locate the lower part of the thyroid cartilage and move the larynx in a rostral direction (Fig. 4). Because the



Fig. 4. The examiner's left hand is located at the lower part of the larynx to move it upwards and also rotate it in an anticlockwise direction, and thus present the interarytenoid groove to the examiner's right index finger.

neck is flexed, there may be limited space for the left hand at the front of the neck. An alternative way of controlling the larynx is to apply the thumb across the neck to produce the required rostral movement (Fig. 5).

In order to outline the interarytenoid groove, it is necessary, as with the other tests, to move the index finger into the groove and then onto the right arytenoid. This is made possible by a slight anticlockwise rotation of the left hand in addition to its rostral movement. If the thumb of the left



Fig. 5. Neck flexion can restrict the space available for placing the left hand on the larynx. This figure shows an alternative way of controlling the larynx. The thumb of the left hand is applied across the lower larynx and moved rostrally. Instead of the usual rotation that is performed by the left hand, the larynx is displaced towards the left of the midline to allow the examining finger access to the interarytenoid groove.

hand is used, the appropriate additional manoeuvre is to displace the larynx from the midline slightly, to the patient's left side. Either of these movements allows the tip of the right index finger to feel round to the right arytenoid and thus delineate the boundaries of the interarytenoid groove. A positive test is confirmed when the tracheal tube is clearly felt to lie immediately anterior to the interarytenoid groove (Fig. 3).

Nasal intubation. Only the side test and mid test are suitable for use with nasal intubation. If the neck flexion used with the mid test does not allow enough room for this manoeuvre, the side test must be used instead. The main problem found when these tests are applied to nasal intubation, is the degree to which the nasotracheal tube presses the larynx against the posterior wall of the pharynx, although this may vary with the design of the tracheal tube. To overcome this effect, the larynx must be lifted forward as has been described elsewhere for introduction of a nasogastric tube.^{3,4} Taking the thyroid cartilage between the thumb and index finger of the left hand, the larynx is lifted forward and additional rostral and rotational movements are used as outlined above. Identification of the interarytenoid groove should then be straightforward, since the remaining part of the technique is similar.

Patients. Three separate studies were undertaken. Only adults (16 years or older) were included in the studies. Any clinical features that suggested the possibility of difficult intubation were noted when the patients were seen pre-operatively. Dentition was recorded; dental block was defined as the presence of any or all of the left lower molar teeth. The view of the vocal cords at laryngoscopy was graded 1 to 4 as described by Cormack and Lehane.⁵

In study 1, one author (P.C.) examined 50 consecutive male patients who exhibited dental block and presented for general surgical operations. All three tactile tests were performed on each patient. Study 2 consisted of two series each of 100 consecutive patients undergoing tracheal intubation. The two authors with small hands (W.A.H. and S.P.) undertook the tests on these patients; the majority of those studied by S.P. were undergoing obstetric procedures

whereas the majority of those studied by W.A.H. were general surgical patients. In study 3 (nasal intubation) the right nostril was used on each occasion, and testing was with the modified mid and side tests. Almost all of these patients presented for dental procedures.

During the period of the studies, colleagues were kind enough to inform one of the authors when a difficult intubation was anticipated (usually because intubation had been noted previously to be difficult). One author attended each of these intubations and performed the tactile tests.

Results

Table 1 indicates the hand size of each of the authors.

Table 1. Dimensions of authors' hands.

Author	Index finger (mm)*	Middle finger (mm)†	Palm width (mm)‡	Glove size
W.A.H.	72	77	80	6
S.P.	70	76	80	6
P.C.	86	91	87	7½

* Index finger length: distance from tip to level of web between index and middle fingers.

† Middle finger length: distance from tip to level of web between middle and ring fingers.

‡ Palm width: width of palm at level of the metacarpo-phalangeal joints.

In study 1, the mid test was positive in all patients and the side and central tests were positive in 74% and 64%, respectively. The mid test provided the only positive confirmation of correct placement of the tracheal tube in 11 patients. Two patients presented difficulty in intubation (both grade 3, epiglottitis only seen).

Table 2. Test scores for study 2 (small hands series, oral intubation). Examiners S.P. and W.A.H.

	Examiner	
	S.P.	W.A.H.
Number in study	100	100
Mean (SD) age, years	45 (22)	46 (18)
Male/female ratio	28/72	44/56
Male/female with dental block *	12/54	30/35
Mid test positive	95	98
Side test positive	96	83
Central test positive	78	NA †
No confirmatory test	3	1

* Male/female with dental block, refers to the sex ratio in patients in whom dental block was also present.

† No central test studies performed in this series.

Table 2 shows the results of study 2. If the results from both anaesthetists with small hands are combined, the position of the tracheal tube could be confirmed in 98% of patients.

The results of the tests after nasal intubation (study 3) are shown in Table 3. Once again, the mid test provided a

Table 3. Test scores for study 3 (small hands, nasal intubation).* Examiner W.A.H.

Number in study	50
Mean (SD) age, years	25 (10)†
Mid test positive	48 (96%)
Side test positive	45 (90%)
No confirmation	2 (4%)

* All patients were intubated via the right nostril and tested by the examiner standing to the patient's left side.

† No patient was less than 16 years old.

high rate of success. In no case did flexion of the neck limit access sufficiently to make lifting the larynx forward with the left hand difficult.

Table 4. Experience with difficult laryngoscopy.

	Examiner		
	S.P.	W.A.H.	P.C.
Number of cases*	3	6	5
Emergency Caesarean sections	2	0	1
Both mid and side tests positive	2	3	2
Mid test only positive	0	2	2
Side test only positive†	0	0	1
Neither test positive‡	1	1	0

* The central test was not much use in any of these cases.

† The mid test had not been discovered when this patient was seen.

‡ In each case the patient was described as having a short, muscular 'bull neck'.

Table 4 reviews the combined experience of the authors with patients who presented with difficult laryngoscopy during the period of the studies. Difficult laryngoscopy should be considered more precise terminology than difficult intubation in this connexion. The laryngoscopy was grade 3 in each case (i.e. epiglottis only seen) and an introducing stilette was used to effect intubation. Again the central test never added to results that could be attained otherwise. In the two cases where the tests failed to confirm placement, both patients had a short muscular neck ('bull neck').⁶ One of these failures occurred when the author concerned had limited experience with the tests.

Discussion

A comparison of the results from study 1 and those from the previous investigation² is shown in Table 5. In patients

Table 5. Test scores for males with dental block* (oral intubation). Examiner P.C.

	Current series	Previous series†
Number in study	50	29
Mean (SD) age, years	52 (17)	46 (18)
Mid test positive	50 (100%)	NA‡
Side test positive	37 (74%)	19 (66%)
Central test positive	32 (64%)	12 (41%)
No confirmation	0 (0%)	5 (17%)

* Dental block was defined as the presence of any or all of the left lower molar teeth.

† This represents the combined results in the previous report (if the mid test had not been available for the current series the 'No confirmation' score would have been 11 (22%)).

‡ NA, not applicable.

with dental block, the mid test appears to provide the most reliable method of confirming correct placement of the tracheal tube.

In Table 6 the characteristics of the three tactile tests are noted to allow direct comparisons. Most of these are obvious, but special attention should be drawn to the fact that landmarks to determine the actual location of the examining finger prior to location of the target are more evident with the side test than with the mid test. In obstetric cases there is greater likelihood of difficult access to the neck, which might have implications for the mid test. Despite this, S.P. recorded similar scores for the mid and side tests (Table 2). On only one occasion overall was the central test positive when the others were negative.

The results confirm a clear clinical impression that the new mid test is an important addition to the series of tactile tests reported previously. The scores recorded by W.A.H. and S.P. show that anaesthetists who have short hands should have little difficulty in using the tests and that the mid test was the most reliable. In the previous paper,² measurements were reported for the distances from the corner of the mouth to the hyoid (mean 84.6 mm, SD 9.5) and from the upper incisors/gums to the tip of the epiglottis (mean 86.3 mm, SD 13). These distances exceed the lengths of the middle fingers of both authors with small hands. However, a number of factors influence the ease with which the interarytenoid groove may be reached.

It is helpful to think in terms of a target (the interarytenoid groove) and how the tests decrease the effective distances to it. It might be considered obvious that the factors listed in Table 7 would lead to a distance reduction, but it is not a simple matter to quantify the contribution each makes because of the number of variables that need to be taken into account.

The starting point at which the examining finger first enters the mouth is obviously important; no distance reduction is achieved at this stage with the central test. Clearly, the likelihood of reaching the interarytenoid groove is increased if the metacarpo-phalangeal joint enters the mouth, and this occurs most commonly with the mid test. The distance reduction due to upward movement of the larynx is self-evident and similar for each of the tests. Forward movement of the tongue has been recognised as important in distance reduction during tracheal intubation in the Treacher-Collins syndrome.⁷ Some movement of the tongue anteriorly is possible with each of the tests but it occurs to the greatest degree with the mid test.

Neck flexion/extension and axial rotation movements are an obvious advantage in the clinical setting. Each of the authors noted that, in general, the greater the displacement from the neutral position the easier it was to perform each of the tests. This applied particularly to the degree of flexion or extension with each test and also to the degree of axial rotation using the mid test.

Overall, the maximal advantage gained from this combination of factors favours the mid test.

Difficult laryngoscopy/intubation. The purpose of investigating tactile tests was to identify their place in confirming the correct placement of the tracheal tube when direct

Table 6. Comparison of the principal tactile tests.

	Side test	Central test	Mid test
Examining digit	Index	Middle	Index
Neck flexion/extension	Extension	Extension	Flexion
Rotation to side	15°	Not required	60°
Dental block important	Yes	(Yes)	No
Easy anatomical landmarks	Yes	(Yes)	No
Position for tooth guard*	Upper left molars	Upper incisors	Upper left premolars
Special indications	Obstetrics	Wide angle mandible†	Males with dental block
Success overall, small hands	83-96%	78%	95-98%
Success overall, large hands	90-96%	71-76%	100%

* Tooth guard recommended for sharp teeth and males with dental block.

† This relates to distance between the molars on the two sides of the jaw.

Table 7. Factors affecting ease of reaching the interarytenoid groove with the examining finger.

	Side test	Central test	Mid test
Examining digit	Enters rear of mouth	Takes longest route	Displaces tongue
Metacarpophalangeal joint enters mouth	No	Possible	Likely
Larynx moved upwards	Yes	Yes	Yes
Larynx moved anteriorly	(Yes)	(Yes)	Yes
Neck flexion/extension	Extension	Extension	Flexion
Axial neck rotation	(Yes)	No	Yes

laryngoscopy is impossible. Experience with these tests should be considered mandatory before they are used in these circumstances. This is perhaps most important in the case of the mid test, in which there are fewer landmarks to guide the finger.

The results in Table 4 justify the interest in tactile tests. Correct placement now confirmed in all three cases of Caesarean section. In some cases, there were clinical features which suggested that intubation might be difficult, but in seven patients, the pre-operative assessment revealed no abnormalities. The two patients in whom confirmation of placement was not possible had short muscular necks. This condition was found in one other difficult laryngoscopy patient, in whom the mid test was positive.

Practical considerations. In most patients, the mid test provides a confirmation of correct placement of the tracheal tube. The side test should be considered in obstetric situations where flexion of the neck may make manoeuvres with the left hand difficult. A limited range of neck movements may, of itself, suggest which test is appropriate. The central test should be considered only for patients with a wide mouth and good mouth opening. Each test usually takes less than 5 seconds to perform. Testing in difficult patients requires a clear understanding of the principles of distance reduction.

Acknowledgments

The authors are grateful to anaesthetic colleagues who alerted us to patients who were expected to present a difficult intubation.

References

1. BIRMINGHAM PK, CHENEY FW, WARD RJ. Esophageal intubation: a review of detection techniques. *Anesthesia and Analgesia* 1986; **65**: 886-91.
2. CHARTERS P, WILKINSON K. Tactile tracheal tube placement test. A bimanual tactile examination of the positioned tracheal tube to confirm laryngeal placement. *Anaesthesia* 1987; **42**: 801-7.
3. SELLERS WFS. Insertion of nasogastric tubes. *British Journal of Anaesthesia* 1979; **51**: 73.
4. PEREL A, YA'ARI Y, PIZOV R. Forward displacement of the larynx for nasogastric tube insertion in intubated patients. *Critical Care Medicine* 1985; **13**: 204-5.
5. CORMACK RS, LEHANE J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39**: 1105-11.
6. MURRIN KR. Intubation procedure and causes of difficult intubation. In: LATTO IP, ROSEN M, eds. *Difficulties in tracheal intubation*. Eastbourne: Baillière Tindall/W.B. Saunders, 1985: 75-89.
7. MIYABE M, DOHI S, HOMMA E. Tracheal intubation in an infant with Treacher-Collins syndrome—pulling out the tongue by a forceps. *Anesthesiology* 1985; **62**: 213-4.

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Tracheal intubation in the presence of an unstable cervical spine

We read with interest the case report by Drs Eason *et al.* (*Anaesthesia* 1987; 42: 745–9). We agree with the authors that this is a difficult case and there are no easy choices, but there are a few points in the management with which we disagree.

We consider that cricoid pressure should be avoided in patients with unstable cervical fractures because it is both ineffective and potentially dangerous for the following reasons.

The cervical spine is normally a rigid structure which

would allow adequate pressure to be applied on the cricoid cartilage to occlude the oesophagus. Wraight *et al.*¹ have demonstrated that a force of at least 44 N is required to prevent regurgitation of gastric contents.

The position necessary for effective cricoid pressure requires that the head and neck be fully extended.²

Any pressure on an unstable cervical spine increases the risk of further displacement, which may result in spinal cord damage.

The best way to anaesthetise this patient in our opinion

All correspondence should be addressed to Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, United Kingdom.

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would be to do an awake tracheal intubation with a fibre-optic bronchoscope. It would also be acceptable to do the intubation under direct laryngoscopy or by the blind nasal route. There are two disadvantages of tracheal intubation after the induction of general anaesthesia. Feedback from the patient about any pressure on the cord during intubation is lost and protective muscle spasm around the fracture site is no longer present.

The authors are quite right to point out that aspiration becomes a serious risk in a heavily sedated patient with an anaesthetised larynx. However, this risk can be minimised by not sedating the patient and placing a suction catheter in the pharynx as soon as the larynx is anaesthetised. Sedation is often used to facilitate awake tracheal intubation, but it is not essential to the success of the procedure. We often perform tracheal intubation without any sedation, with no apparent patient discomfort.

Intubation with a fibreoptic bronchoscope is easier by the nasal route because there is no sharp turn to negotiate. The tongue does not fall back in an awake patient and as soon as the tip of the bronchoscope reaches the posterior pharynx the vocal cords should be visualised.

We have practised anaesthesia on both sides of the Atlantic and can understand the reluctance to do an awake intubation. In the UK we all receive instruction on how to do tracheal intubation under topical anaesthesia but few get the opportunity to actually see it performed, let alone do one themselves. In the USA awake intubation is fairly frequent, perhaps because of the greater number of morbidly obese patients. This results in a greater exposure to the technique for those persons involved in the delivery of anaesthesia. We have now performed a number of these procedures and have always found that patient acceptance is good once they know what to expect. The experience of an awake intubation should be no worse than having a nasogastric tube passed once the mucosa has been adequately anaesthetised.

The University of Iowa Hospitals,
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G.D. KAMAL
J.S.T. SUM PING
D. PATHAK

Acquired C₁ esterase inhibitor deficiency

The report by Razis *et al.* (*Anaesthesia* 1986; 41: 838-40) on the management of patients with acquired C₁ inhibitor deficiency for surgery prompts us to report the successful management of two cases which used different methods.

Case 1. A 32-year-old female with a follicular lymphoma and associated untreated acquired C₁ inhibitor deficiency presented for splenectomy. She was given 5 units of fresh frozen plasma (FFP) before operation, 3 during and 1 unit 4-hourly for 24 hours after operation. Anaesthesia was induced with thiopentone 225 mg and tracheal intubation was facilitated with suxamethonium 50 mg. Anaesthesia was maintained with N₂O, halothane, fentanyl, and pancuronium. She had no problems related to either angio-oedema or thrombosis. Her complement levels are shown in Table I.

References

1. WRAIGHT WJ, CHAMNEY AR, HOWELLS TH. The determination of an effective cricoid pressure. *Anaesthesia* 1983; 38: 461-6.
2. SELICK BA. Cricoid pressure to control regurgitation of stomach contents during induction of anaesthesia. *Lancet* 1961; 2: 404-6.

A reply

Thank you for the opportunity to reply to Drs Kamal, Sum Ping and Pathak. Their point concerning our use of cricoid pressure is well taken: insofar as our patient's neck was not extended and compression was applied somewhat cautiously, we have to accept their criticism that it was probably ineffective, particularly if the force required to prevent passive regurgitation is as great as is stated.

It is also our opinion that the best way to anaesthetise our patient would have been to do an awake tracheal intubation with a fibreoptic bronchoscope, provided that we had been confident of our ability to perform this manoeuvre without provoking coughing, vomiting, gagging or panic in this unfortunately uncooperative patient. We are less convinced, however, that blind nasal intubation under topical anaesthesia would have been safe.

We congratulate Dr Kamal and colleagues on their expertise, but sadly many anaesthetists in the United Kingdom, amongst whom we number ourselves, cannot claim to be able to perform awake intubation without the risk of the sort of movements which would have been dangerous in our patient. Unless and until a programme of training has elevated UK skills to a level comparable to that which it is claimed exists in the USA we fear that statements to the effect that fibreoptic awake intubation is the only way to manage such patients may compel those who do not have such expertise to attempt the procedure with disastrous results. To be honest, we are not even confident that we could pass a nasogastric tube in a frightened patient with an unstable neck fracture and a full stomach without provoking coughing and straining.

King's College Hospital,
London SE5 8RX

J. EASON
C. SWAINE

Table 1.

	Case 1		Case 2		
	Before FFP	After FFP	Before C ₁ inhibitor	After	2 days
C ₁ inhibitor	63	370	202	331	426
C ₄ inhibitor	0	286	47	41	208
Normal values C ₁ inhibitor 149-421 µg/ml					
C ₄ 199-1800 µg/ml					

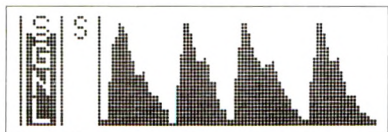
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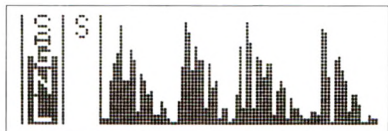
"...interference, such as from a pulsatile light source, may cause erroneous SaO_2 readings. An oximeter with a pulse waveform, rather than just bouncing dots, may be better able to detect interference because it can indicate a discrepancy from the norm."

"A well-designed oximeter should be able to detect power line frequency, compensate for background light flicker such as with fluorescent lamps, and display a true pulse waveform rather than bouncing dots."

Jeffrey B. Gross, M.D.
Associate Professor of Anesthesia
University of Pennsylvania,
Philadelphia, Pennsylvania



In the presence of a clean, physiological signal, the waveform is smooth, uniform and pulsatile in shape. The higher the signal strength indicator, the stronger the signal.



In the presence of interference, the waveform shows a noisy plethysmograph.

"In several of our studies of hypoxemia where it was important that the researchers and clinicians be blinded from the results, we found the waveform to be useful to distinguish real data from artifact."

Daniel B. Raemer, Ph.D.
Assistant Professor of Anesthesia (Bioengineering)
Brigham and Women's Hospital
and Harvard Medical School
Boston, Massachusetts

"Observing the waveform is a vital aid to instantly rejecting artifact and is useful in providing extra data about the patient's cardiovascular system."

Richard Morris
M.B.B.S., F.F.A.R.C.S.
Staff Specialist
Department of Anaesthesia
and Intensive Care
Prince Henry Hospital
Little Bay, New South Wales
Australia

"Because the SaO_2 produced by the pulse oximeter is based on pulsatile absorbance of light, the pulsatile waveform is the essential quality control indicator."

William T. Cecil, R.R.T.
Coordinator
Respiratory Care Services
St. Luke's Hospital
Kansas City, Missouri

"I feel secure that the information I am getting is based on a good pulse. I can trust the reading."

Gayle Miller, R.N.
Unit Administrator
Post-Anesthesia Care Unit
University Hospital
University of Colorado
Health Sciences Center
Denver, Colorado

"We would not consider purchase of a saturation monitor that did not have a waveform."

Anneke Meursing, M.D.
Anesthesia Department
Sophia's Children's Hospital
Rotterdam, Netherlands

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Jeffrey A. Neilsen, C.R.N.A.
Staff Nurse Anesthetist
Christian Hospital
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St. Louis, Missouri

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¹Costarino AT, Davis DA, Keon TP: Falsely normal saturation reading with the pulse oximeter. *Anesthesiology* 67:830-831, 1987. ²Hanowell L, Eisele JH Jr, Downs D: Ambient light affects pulse oximeters. Correspondence. *Anesthesiology* 67:864-865, 1987. ³Swedlow DB, Running V, Feaster SJ: Correspondence. *Anesthesiology* 67:865, 1987. ⁴Block FE Jr: Interference in a Pulse Oximeter from a Fiberoptic Light Source. *Journal of Clinical Monitoring*, July 1987, pp 210-211. ⁵Brooks T, Paulus D, Winkle W: Infrared Heat Lamps Interfere with Pulse Oximeters. *Anesthesiology* 61:630, 1984.

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suxamethonium 100 mg. Anaesthesia was maintained with N₂O, enflurane and atracurium. Her complement levels are shown in Table 1.

The first patient showed a good response to FFP with both C₁ inhibitor and C₄ levels in the normal range in the peri-operative period. The second patient's normal treatment provided C₁ inhibitor levels in the normal range but the low C₄ level indicated the presence of complement activation. C₁ inhibitor concentrate did raise the C₁ inhibitor level immediately but the C₄ level rose only slowly over the first 2 days of treatment (there is no C₄ in the C₁ concentrate). These results show that C₁ inhibitor concentrate does not reduce complement activation to a greater extent than does danazol. It is not obvious from this patient that evidence of complement activation, as assessed by a low serum C₄ level has any relationship to attacks of angio-oedema.

The second patient had C₁ inhibitor levels in the normal range before treatment so we cannot guarantee that C₁ inhibitor concentrate alone would be sufficient to give protection, although the rise in C₁ inhibitor level seen in this patient suggests it would. The administration of FFP results in increased serum levels of C₁ and C₄ and may provide an alternative regimen.

We suggest that either FFP or C₁ inhibitor concentrate are suitable for prophylaxis in acquired C₁ inhibitor deficiency during surgery and that the immediate rise in C₁ inhibitor levels seen offers advantages over danazol, which takes several days before an effect is seen.

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J.L. PLENDERLEITH
T. ALGIE
K. WHALEY

A reply

We thank Drs Plenderleith, Algie and Whaley for their interest in our case report, and for the opportunity to comment.

Danazol has been best investigated in terms of prophylaxis; we regard it as the drug of choice. Its effect lasts up to 12 days¹ so we consider the use of C₁ inhibitor concentrate in Case 2 unnecessary. We agree that the low serum C₄ level bears no relationship to attacks of angio-oedema which is why we do not advocate the use of plasma inhibitors peri-operatively.

The use of FFP in Case 1 appears reasonable from an immunological point of view. However, in a patient with no history of angio-oedema it may be unnecessary but could be given in the event of problems.

St George's Hospital,
London SW17 0QT

I. FINDLEY
P. RAZIS

Reference

1. GELFAND JA, SHERINS RJ, ALLING DW, FRANK MM. Treatment of hereditary angioedema with danazol. *New England Journal of Medicine*. 1976; **295**: 1444-8.

Asystole not corrected by glycopyrronium

Glycopyrronium is being increasingly used as a substitute for atropine in anaesthetic practice. We report the following case to alert anaesthetists to the inadvisability of using this drug to correct life threatening bradycardia.

A 30-year-old labourer who weighed 73 kg was admitted with a stab wound to his scrotum. One hour before surgery he received pethidine 60 mg intramuscularly. The operation was performed after lignocaine infiltration; an anticholinergic was not administered. The patient complained of severe pain whilst the wound in his tunica vaginalis was being sutured. Almost immediately his heart rate dropped dramatically and asystole occurred. Five seconds after asystole glycopyrronium, which had already been drawn up into a syringe, was given in a dose of 0.4 mg into a free flowing intravenous line. External cardiac massage and oxygen administration were started immediately. Sinus rhythm had not returned within one minute so atropine 1.0 mg was given intravenously. An immediate response occurred and the patient recovered without further complications.

One of the main advantages of glycopyrronium is the cardiovascular stability when used with neostigmine for reversal of neuromuscular block. This results from the slower onset time of glycopyrronium compared to that of atropine.¹ It is this gradual onset which makes it unsuitable for treating the type of severe bradycardia illustrated in this case.

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A.H. Robins Co Ltd,
Crawley, West Sussex

D.A. COZANITIS

C.J. JONES

Reference

1. MIRAKHUR RK, JONES CJ, DUNDEE JW. Effects of intravenous administration of glycopyrrolate and atropine in anaesthetised patients. *Anaesthesia* 1981; **36**: 277-81.

On the use of suxamethonium for open eye cases

Abbott notes, in a recent report on the use of vecuronium to facilitate tracheal intubation for emergency eye surgery, (*Anaesthesia* 1987; **42**: 1008-12) the potential advantages of suxamethonium for this purpose were it not for the suggestion that suxamethonium increased intra-ocular pressure which may lead to vitreous herniation.

Libonati *et al.*¹ reported on 100 patients with open eye injuries who received suxamethonium without adverse effects. They state that this technique has been used successfully in 250 cases per year for 10 years. They note that no actual case of vitreous herniation due to suxamethonium was found in their literature search.

The need for a rapid onset of flaccid paralysis for tra-

cheal intubation in patients with a full stomach and open eye injury is clear. The report of a large series of patients who were safely treated in this manner suggests that suxamethonium may be the relaxant of choice for these cases.

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M. SOSIS

Reference

1. LIBONATI MM, LEAHY JJ, ELLISON N. The use of succinylcholine in open eye surgery. *Anesthesiology* 1985; **62**: 637-40.

The lightwand as an atraumatic alternative to blind stylet intubation

Young and Robinson¹ report a case of cellulitis, dysphagia and systemic toxicity after a difficult tracheal intubation. Presumably, the ventral wall of the trachea or larynx was perforated with the guide stylet. Blind stylet intubation has also been associated with perforation of the oesophagus, hypopharynx and piriform fossa.²

Many alternatives to the blind stylet method have been developed. The authors¹ mention the use of a fibre-optic laryngoscope, guided blind intubation after puncture of the cricothyroid membrane or blind nasal intubation. This list could be lengthened considerably, since every anaesthetist encounters difficult intubations occasionally and must find ways of dealing with this problem. Novel approaches to difficult intubation continue to be published regularly.

May we add the Tube Stat (the Intubation Stylet, manufactured by Concept Inc., 12707 US South, Clearwater, Florida, 34547-7295 USA) lightwand technique to the top of this list. This method first described some time ago has been gaining recognition in the last few years³⁻⁵ and consists of special lightwands constructed for anaesthetic use in both oral and nasal intubations.^{3,4} We have used the lightwand in routine surgical cases and, after familiarisation with the technique, we find it to be rapid, reliable and atraumatic. Our experience agrees with others.^{3,4}

There are several reports^{3,5} about the effectiveness of this technique in cases of difficult or failed laryngoscopic intubation. The lightwand is superior in terms of intubation time, average number of intubation attempts and incidence of injury in comparison with blind nasal intubation.⁵ Intubation can be accomplished in a fully paralysed patient

which minimises the risk of damage to the vocal cords, and transillumination of the neck, not breath sounds, guide the operator to the trachea.

The equipment needed is cheap, reliable and re-useable and the technique can be mastered quickly. Regular practice in routine cases is a prerequisite for successful intubation of the infrequent difficult case.

The lightwand is a useful, atraumatic alternative approach to the challenge of failed laryngoscopic intubation when difficulty is encountered.

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8952 Schlerten,
Switzerland

S. ZBINDEN
G. SCHÜPFER

References

1. YOUNG PN, ROBINSON JM. Cellulitis as a complication of difficult tracheal intubation. *Anaesthesia* 1987; **42**: 569.
2. A WENGEN DF. Piriform fossa perforation during attempted tracheal intubation. *Anaesthesia* 1987; **42**: 519-21.
3. WILLIAMS RT, STEWART RD. Transillumination of the trachea with a lighted stylet. *Anesthesia and Analgesia* 1986; **65**: 542-3.
4. ELLIS DG, JAKYMEC A, KAPLAN RM, STEWART RD, FREEMAN JA, BLEYAERT A, BERKEBILE PE. Guided orotracheal intubation in the operating room using a lighted stylet: a comparison with direct laryngoscopic technique. *Anesthesiology* 1986; **64**: 823-6.
5. FOX DJ, CASTRO T, RASTRELLI AJ. Comparison of intubation techniques in the awake patient: the Flexi-lum_r surgical light (lightwand) versus blind nasal approach. *Anesthesiology* 1987; **66**: 69-71.

Bronchospasm after neostigmine

On three occasions in the last 18 months I have had patients who unexpectedly became wheezy shortly after reversal of neuromuscular blockade, twice after atracurium once after vecuronium. On each occasion approximately 2.5 mg neostigmine and 0.3-0.4 mg glycopyrronium were administered. One patient had a history of asthma but this had not occurred for many years. The anaesthetics up to the reversal had been quite normal with no evidence of bronchospasm.

The mechanism of this response was not clear at first but after the recent episode it occurred to me that perhaps the glycopyrronium acted too slowly to block the muscarinic effects of neostigmine. This reaction might be more common with the new neuromuscular blockers which lack intrinsic anticholinergic action and did not happen, as far as I remember, after atropine, which has a more rapid onset of action.

The three patients recovered after about 20-30 minutes

with no untoward effects, although their condition gave cause for some concern initially. They all settled on oxygen by mask, Ventolin nebulizer solution and intravenous hydrocortisone. Chest X rays were normal, apart from perhaps some hyperinflation.

A.H. Robins are now marketing a combined preparation and I wonder if this will be safe under all circumstances? It would seem that perhaps a small minority of patients are particularly susceptible to the muscarinic effects of neostigmine if inadequately blocked. Perhaps it should be recommended that glycopyrronium should be administered on its own a few minutes before the combined preparation to avoid these problems.

Princess Elizabeth Hospital,
St Martin,
Guernsey

C.I. PRATT

Sales promotion

The fact Robins are promoting their products Robinul and Dopram together with neostigmine and atropine in a special box designed for use in the operating theatre disturbs me.

This seems to be dangerous sales promotion. The similarity between the ampoules of glycopyrronium 3 ml and doxapram 5 ml is such that it will not be long before doxapram is used instead of glycopyrronium combined with neostigmine, to reverse neuromuscular blockade, obviously with disastrous results. The ampoules are the same size, one has blue writing on it, the other green. Of course it is

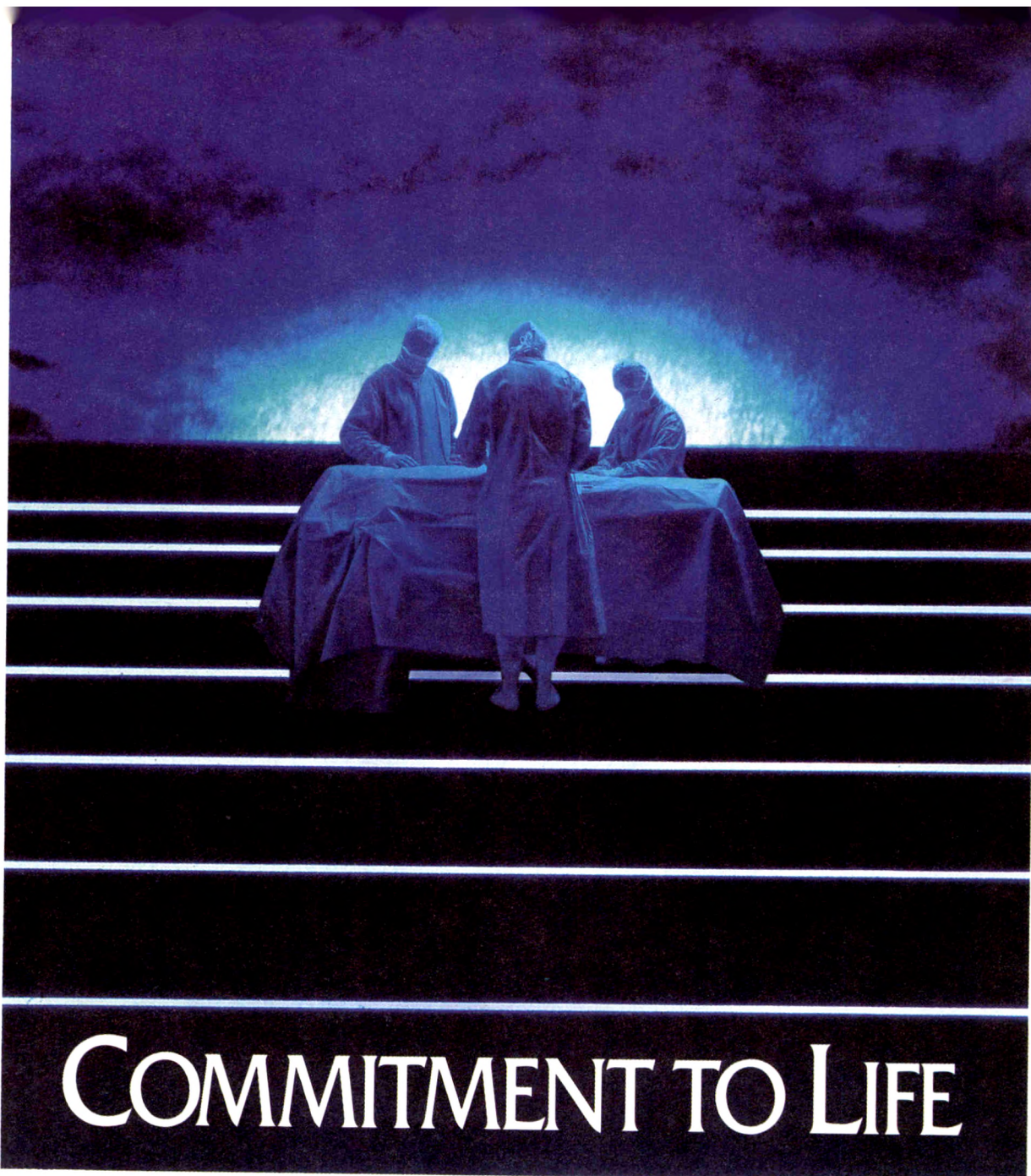
our responsibility to read and check the labels of any drug but if there is the possibility of confusion a mistake will happen.

Neath General Hospital,
Neath,
West Glamorgan SA11 2LQ

P.A. SCHWARZ

A reply

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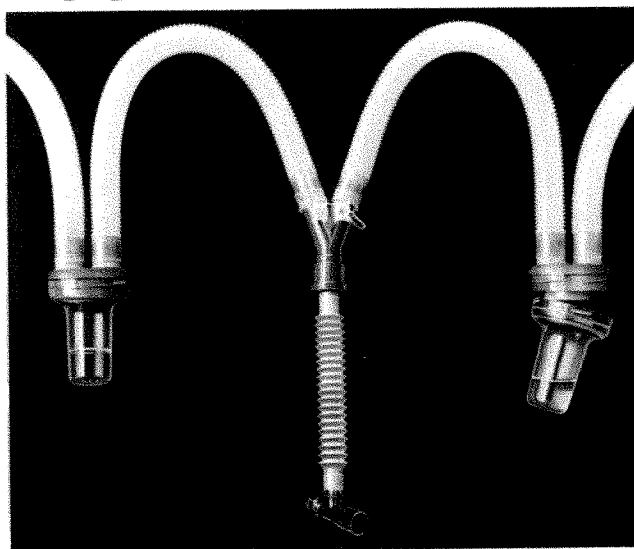
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anaesthetists in response to requests for such an item. It is intended to be used as a convenient container in which anaesthetists may keep ampoules of any drug.

Stick-on labels are supplied with the box to facilitate this and these are printed with the approved names of a wide number of drugs in common use by anaesthetists: doxapram, glycopyrronium and glycopyrronium/neostigmine being three of these. The trade names Robinul and Dopram are printed on the lid of the box, but the choice of drugs and labels is left to the anaesthetist.

We feel that to take an ampoule from this box presents no greater risk than to take an ampoule from any already opened box. If your readers believe that this is not the case may we ask that they write to this company so that we may assess how many of Dr Schwartz's colleagues share his misgivings.

A.H. Robins Company,
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J.F. HORT

A complication of ilio-inguinal block for inguinal hernia repair

Ilio-inguinal and iliohypogastric nerve blocks are employed to supplement general anaesthesia and to ensure post-operative pain relief and rapid return to normal activities in patients undergoing inguinal hernia repair. This usually results in sensory block with no motor deficit. However, we have encountered two cases where motor weakness involving the quadriceps femoris, accompanied by sensory loss in the distribution of the femoral nerve has occurred postoperatively.

The first case was that of a fit 74-year-old man scheduled for repair of left inguinal hernia. General anaesthesia was induced with thiopentone and maintained with oxygen, nitrous oxide and enflurane. The ilio-inguinal and iliohypogastric nerves were blocked by inserting a 20-G spinal needle 2 cm medial and inferior to the anterior superior iliac spine and injecting plain bupivacaine 0.375% 15 ml immediately after penetration of the aponeurosis of the external oblique muscle.¹ This ensured good intra-operative conditions and the patient required no opiate analgesia at any time postoperatively.

Eight hours after surgery he complained that his left leg was weak on attempting to get up out of bed and that it would not support his weight. Clinical examination revealed weakness of knee extension and loss of sensation in the distribution of the femoral nerve. The motor block persisted for approximately 12 hours and the sensory block for 16 hours.

The second case was that of a 57-year-old man who underwent a similar procedure under general anaesthesia and ilio-inguinal blockade as described above. He developed weakness of quadriceps femoris and sensory loss in the distribution of the femoral nerve. Again this persisted for about 12 hours.

Inadvertent femoral nerve block during ilio-inguinal and iliohypogastric blockade has been reported previously in paediatric practice. Shandling and Steward,² found that the incidence of this complication was 2% in a series of 156 children. They suggested that this was due to the local anaesthetic solution tracking within fascial planes, and that it could be avoided by the use of a more dilute solution of bupivacaine. Roy-Shapira *et al.*³ also reported this complication and suggest that local anaesthetic can diffuse readily into the peri-operative field in paediatric practice but did not specify the anatomical site.

We have been unable to find any report of this complication of ilio-inguinal block in adults. Nerve block for

inguinal herniorrhaphy is performed by deposition of local anaesthetic beneath the aponeurosis of external oblique; this ensures that the ilio-inguinal and iliohypogastric nerves are blocked. The femoral nerve however, after emerging from the lumbar plexus, lies on the posterior abdominal wall descending in the groove between psoas major and iliacus muscles behind the iliac fascia. The anterior and posterior abdominal walls meet the thigh at the groin and their fascial linings, the transversalis and iliac fascia respectively, become continuous with one another. The aponeurosis of external oblique ends as a free inrolled margin which forms the inguinal ligament and this is fused to the transversalis fascia at the anterior surface of the thigh. The femoral nerve lying behind iliac fascia enters the thigh below the inguinal ligament and lateral to the femoral sheath. Deposited local anaesthetic is free to diffuse between external oblique aponeurosis and transversalis fascia but it is apparent therefore that local anaesthetic deposited in this fascial plane, in some patients at least, must be able to traverse fascial planes and track downwards in order to produce a femoral nerve block.

It is likely that the volume of local anaesthetic injected will be important when such complications are considered; larger volumes will increase the chances of diffusion outside the immediate field of the block, and the concentration of solution will determine the incidence of motor blockade as mentioned by Steward.² Although uncommon the possibility of this occurrence should be borne in mind by the clinician. Patients may justifiably be alarmed by an apparent paresis and it may be appropriate to forewarn nursing staff of this possibility and to emphasise its transitory nature.

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References

1. ERIKSON E. *Illustrated handbook of local anaesthesia*. London: Lloyd Luke, 1979.
2. SHANDLING B, STEWARD DJ. Regional analgesia for post-operative pain in pediatric outpatient surgery. *Journal of Pediatric Surgery* 1980; 15: 477-80.
3. ROY-SHAPIRA A, AMOURY RA, ASHCRAFT KW, HOLDER TM, SHARP RJ. Transient quadriceps paresis following local inguinal block for postoperative pain control. *Journal of Pediatric Surgery* 1985; 20: 554-5.

On the hazards of priming

In their report of two patients who displayed respiratory distress due to clinical paralysis after vecuronium 13.7 and 10 µg/kg, Cherala *et al.* (*Anaesthesia* 1987; 42: 1021) state that priming is a safe technique in nonpregnant patients. The authors cite Foldes¹ and Taboada *et al.*² to support the concept that 10-15 µg/kg is a safe priming dose. Foldes¹

presented no data to corroborate his suggestion of priming doses of vecuronium 15-20 µg/kg. The findings of Taboada *et al.* have been criticised³ since they used extremely heavy sedation which may have masked the effects of priming doses on their patients.

Engback *et al.*⁴ in a study of healthy volunteers have

shown that doses above vecuronium 10 µg/kg should not be administered to awake patients or clinically significant paralysis may occur. They also note marked sensitivity to 5 µg/kg in one patient. My own studies have shown that priming doses of vecuronium⁵ or atracurium⁶ may not be well tolerated and may cause decreases in maximum inspiratory pressure and the inability to sustain 5-second head lift. Furthermore, intubating conditions are not improved as compared to a single dose technique. A case of pulmonary aspiration after priming has recently been described.⁷ Priming may not be a safe technique in patients at risk from pulmonary aspiration and other methods for rapid tracheal intubation are recommended.

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Prolonged neuromuscular blockade with vecuronium in renal failure

We were interested in two recent reports concerning persistent neuromuscular blockade with vecuronium: one adult in renal failure (*Anaesthesia* 1987; 42: 993–5); and one in an infant receiving a vecuronium infusion (*Anaesthesia* 1987; 42: 1020). We should like to add to these a case of prolonged neuromuscular blockade in an adult in acute renal failure who received vecuronium by infusion.

A 47-year-old man was admitted to hospital with a postero-inferior myocardial infarct. He was found to have developed acute mitral regurgitation secondary to papillary muscle dysfunction and became oliguric as a consequence of the resulting hypotension. Urgent cardiac catheterisation showed triple vessel disease; he was therefore scheduled for emergency mitral valve replacement and coronary artery bypass grafts. In view of the severe pulmonary oedema and cardiogenic shock, artificial ventilation of the lungs was started pre-operatively and an intra-aortic balloon inserted. Continuous arteriovenous haemofiltration via the femoral vessels was also instituted in an effort to reduce preload in the presence of continued oliguria. He received sedation with fentanyl for this and increments of pancuronium (4 mg × 3) for relaxation. He was noted to have regained good skeletal muscle power before surgery. Induction was with midazolam 5 mg, fentanyl 500 µg and vecuronium 7 mg; he then received infusions of fentanyl (7 µg/kg/hr) and vecuronium (0.08 mg/kg/hr reduced to 0.04 mg/kg/hr whilst on bypass).

Peritoneal dialysis was commenced after surgery because he was anuric and both the plasma urea and creatinine had risen significantly. Haemofiltration was stopped at this stage. Sedation and ventilation were continued postoperatively for a further 24 hours. He received fentanyl (4–7 µg/kg/hr) and vecuronium (0.08 mg/kg/hr) both by continuous infusion during this period.

The vecuronium was stopped after a total of 30 hours infusion. Six hours later the fentanyl was also stopped. The next morning (18 hours after stopping vecuronium) the patient was noted to be hypertensive with a sinus tachycardia, was sweating profusely and appeared distressed although he was making no respiratory effort. Blood gases were satisfactory but stimulation of the ulnar nerve at the wrist with recording of the evoked compound EMG from the adductor pollicis (Medelec MS6 system) revealed no response to a train-of-four (TOF) and a weak non-sustained tetanic response with a post-tetanic count (PTC) of 9. The

References

1. FOLDES F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs: the priming principle. *British Journal of Anaesthesia* 1984; 56: 663.
2. TABOADA JA, RUPP SM, MILLER RD. Refining the priming principle for vecuronium during rapid-sequence induction of anaesthesia. *Anesthesiology* 1986; 64: 243–7.
3. SOSIS M. On the efficacy of the priming principle with vecuronium. *Anesthesiology* 1986; 65: 120–1.
4. ENGBAER J, HOWARDY-HANSEN P, ORDING H, VIBY-MOGENSON J. Precurarization with vecuronium and pancuronium in awake, healthy volunteers: the influence on neuromuscular transmission and pulmonary function. *Acta Anaesthesiologica Scandinavica* 1985; 29: 117–20.
5. SOSIS M, STINER A, LARIJANI GE, MARR AT. An evaluation of priming with vecuronium. *British Journal of Anaesthesia* 1987; 59: 1236–9.
6. SOSIS M, LARIJANI GE, MARR AT. Priming with atracurium. *Anesthesia and Analgesia* 1987; 66: 329–32.
7. MUSICH J, WALTZ LF. Pulmonary aspiration after a priming dose of vecuronium. *Anesthesiology* 1986; 64: 517–9.

patient's condition improved with sedation. Neuromuscular function was then monitored at approximately 12-hourly intervals. The PTC was 18 though only T1 of TOF was present after a further 24 hours; at 48 hours TOF ratio was 0.4 with PTC of > 30; at 72 hours full neuromuscular function had returned with no depression of TOF.

Peritoneal dialysis continued throughout this time and despite the existence of established renal failure, blood gases and electrolytes (including calcium and magnesium) were within the normal laboratory range. Initially the patient required inotropic support with dopamine and dobutamine; in addition he received regular intravenous doses of netilmicin (100 mg/day), flucloxacillin (500 mg tds) and ranitidine (50 mg tds).

Vecuronium was chosen to provide neuromuscular blockade in this case because it is free from cardiovascular effects, has a short duration of action, lacks cumulation when given by infusion¹ and is reported to be safe in renal failure.² The prolonged recovery (90 hours after the infusion was stopped) described here must reinforce doubts as to the suitability of vecuronium in renal failure, particularly when infused. The patient also received an aminoglycoside antibiotic, netilmicin. This drug has been shown to potentiate existing neuromuscular blockade with vecuronium in the isolated phrenic nerve diaphragm preparation of the rat.³ An interaction with concurrent aminoglycoside therapy cannot therefore be discounted, although it seems that significant prolongation of the action of vecuronium may occur when it is used by continuous infusion in renal failure.

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References

1. MIRAKHUR RK, FERRES CJ, PANDIT SK. Muscle relaxation with an infusion of vecuronium. *Anesthesiology* 1984; 61: A293.
2. BEVAN DR, DONATI F, GYASI F, WILLIAMS A. Vecuronium in renal failure. *Canadian Anaesthetists' Society Journal* 1984; 31: 491–6.
3. RUTTEN JMJ, BOOIJ LHDJ, RUTTEN CLJ, CRUL JF. The comparative neuromuscular blocking effects of some aminoglycoside antibiotics. *Acta Anaesthesiologica Belgica* 1980; 31: 293–306.

A reply

Thank you for the opportunity to reply to this letter. The case quoted reiterates our point that vecuronium should be used with caution in renal failure. We do, however, feel that the dosage used was large for a patient in such poor

condition, without apparently the help of a nerve stimulator to monitor the degree of block.

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Extradural blood patch after an intradural injection

Extradural blood patch has an established role in the management of spinal headache although the exact mechanism by which it acts is not known. One particular problem is to know where the extradural blood exerts its effect.

A patient presented with severe spinal headache after the insertion of implanted lumbar intrathecal catheter system (Port-a-Cath, Pharmacia). The catheter is inserted intrathecally through an 18-gauge Tuohy needle and then tunnelled subcutaneously to the portal which is sited over the anterior lower ribs, usually on the non-dominant side to allow the patients to administer the drug themselves. The patient's headache started within hours of the catheter insertion and did not respond to conventional treatments with liberal fluids and bed rest.

Seven days after catheter insertion an extradural blood patch was performed using 20 ml of blood. The injection was made one interspace lower than the catheter insertion to avoid transfixing the catheter. He was discharged two days later but re-admitted within a further two days with recurrence of headache. A radiculogram was performed on the advice of neurosurgical colleagues with access through the catheter portal in order to exclude major cerebrospinal fluid leak. The films showed the blood patch as a lumbar extradural space-occupying defect (Fig. 1). No major leak was observed so a further blood patch was performed this time using 20 ml one interspace higher than the catheter insertion. This resulted in cure of the headache and the patient was discharged home.

The present case is the only one to date in some 50 insertions in whom post-spinal headache has occurred after insertion of a catheter despite using a large diameter needle (2%). It is of note that one week after the blood patching was performed the effect of an extradural space-occupying mass is still present.

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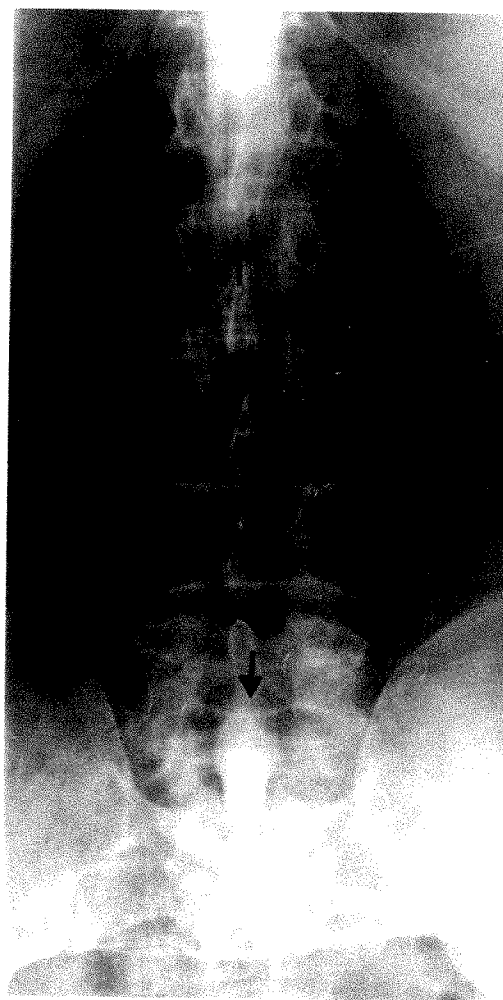


Fig. 1. Anteroposterior and lateral radiculograms which demonstrate the posterior lumbar extradural-filling defect (arrowed).

Anaphylactoid reactions to prilocaine

The recent report (*Anaesthesia* 1987; **42**: 1078-80) of localised reactions to the intravenous injection of prilocaine administered to an isolated forearm in an attempt to produce a Bier's block in two patients invites some criticism. Firstly, the paper begins by stating that 'Numerous reports of adverse reactions to local anaesthetic agents of an apparently immunological nature are to be found in medical journals'. What the paper does not say is that careful analysis of most of these reports shows that the reaction was either to some other component of the solution injected or was not immunological in nature; I believe that both these explanations might be applicable in these cases.

It seems odd to me that an immunological reaction should be so localised in distribution. Presumably localised histamine release would, while the tourniquet was inflated, produce the severe pain described, but if that were the case would there not have been some obvious systemic reaction after tourniquet release? The authors say that any vaso-

active substances would have been inactivated by that time but surely the prilocaine would have triggered further release on its entry to the systemic circulation?

It is far more likely that there was some contaminant in the solution and the absence of a systemic effect from a contaminant could be explained on dilutional grounds. In an exsanguinated limb its concentration could have been great enough to cause tissue irritation but return of blood flow after tourniquet release would then considerably reduce its concentration. The occurrence of two *very unusual* reactions close together in one hospital further raises the possibility of solution contamination. When any reaction occurs in a patient the solution must be retained and subjected to chemical analysis because contamination may occur during manufacture, storage or (most likely) preparation for administration by the clinician. These possibilities would not seem to have been considered.

Even if the authors can clearly explain how a localised

immunological reaction could be associated with the total absence of a systemic one, they have produced no evidence that the reaction was to prilocaine. Allergy to amide local anaesthetics is extremely rare but it is relatively common to preservatives such as the methylhydroxybenzoate which is present in the solution that was used. The possibility that the reaction was to the preservative was considered but of course it is prilocaine that is named in the title. It is also appropriate to point out that Astra Pharmaceuticals market a preservative-free solution of prilocaine specifically for Bier's block, because many authorities advise against the use of a preservative-containing solution.

Finally, what were these patients told about their reactions? If they were informed that they are 'sensitive' or 'allergic' to local anaesthetics it has very serious future implications for them because even the most minor surgery would require general anaesthesia; the evidence presented in this paper does not, in my opinion, warrant this. In the last few years I have seen a number of patients who have been incorrectly labelled as being 'allergic' to local anaesthetics. A full history from the patient (and medical or dental personnel if possible) and then cautious skin testing (intradermal injection of progressively increased concentration of preservative-free solution) followed by treatment under close supervision usually produces the inescapable conclusion that some other factor must have been responsible for the previous reaction. I elicited a systemic response¹ on only one occasion and there was serial immunological confirmation of its nature.

When a patient suffers an adverse drug reaction it is vital that *all* the possible causes are considered and that the case be properly investigated. I know that skin testing is an inexact science but it has a place especially in bizarre reactions such as these. In most cases the 'skin testing' I refer to is really a challenge test that simply reassures the patient that the reaction was not due to local anaesthetic allergy. The risk of a severe reaction exists (so full resuscitation facilities must be available) but the chances of anything happening are so remote that the risk is acceptable.

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Reference

- ¹ BROWN DT, BEAMISH D, WILDSMITH JAW. Allergic reaction to an amide local anaesthetic. *British Journal of Anaesthesia* 1981; 53: 435-7.

A reply

While it is always pleasing to attract attention to case reports we really cannot understand Dr Wildsmith's response since the points he raised are already answered in the report.

Our original report was designed to stimulate anaesthetists who had also encountered this type of phenomenon to regional anaesthetics and thus to obtain some idea of the numbers involved.

Several reports of adverse reactions to local anaesthetic preparations are to be found in the medical literature, though perhaps to describe such reports as numerous was a little exaggerated on our part. A glance through our records for this year shows one Bier's block reaction of this type and seven delayed systemic reactions to epidurals. We agree with Dr Wildsmith that immune reactions are rare and those with the *characteristics* of an immune response but without or unproven antibody involvement are described conventionally as 'anaphylactoid reactions'.

Our tests on the two patients reported indicated no

antibody mediated mechanism for either. There are obvious objections to skin testing particularly when there is no evidence of immune response in the first place. Fisher also considers skin testing of little value with local anaesthetic agents. (See our report).

In terms of impurities the same batches were used on other patients without ill effects. The residua of the solutions used on the patients referred to in our case report were submitted for chemical analysis and no contaminants were found. We did refer to the possibility of preservative involvement but again this implies idiosyncrasy in our two reactants.

As to treatment of the original clinical reactions our experience over several years with the Sheffield based NAARAS (National Adverse Anaesthetic Reactions Advisory Service) confirms that this is the approach used by most anaesthetists faced with this problem. It may well be that release into the general circulation of the prilocaine formulation would cause little further effect as a result of whole-body dilution. We would not like this attempted on ourselves and a wise precaution still appears to be to allow some decay of the drug (in terms of tissue binding) and the preparation of the uncontaminated circulation with H₁ and H₂ antagonists. The latter has been used by other anaesthetists without ill effects.

As to not informing the patient, the evidence of the mishap is clearly evident—are we to pretend it never happened? It was the patient who, being awake, experienced the pain! We believe that NAARAS now has the reputation of being non alarmist and gives sound advice to the anaesthetist on behalf of his patient.

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The allegation by Ruiz *et al.* (*Anaesthesia* 1987; 42: 1078-80) that the painful discolouration of the isolated limb in each of two patients after attempted Bier's block with prilocaine was anaphylactoid in nature is open to doubt. Few would agree with their inference from the literature that immunological adverse reactions to local anaesthetics are not unusual. The immediate pain reported after injection of the prilocaine solution was almost certainly due to the preservative in the preparation which is inappropriate for Bier's block. A preservative-free solution of prilocaine, purpose-made for Bier's block, has been on the market in the UK since February 1984. Attention was drawn in 1983¹ to the need for preservative-free prilocaine as an intravenous regional guanethidine block; it was realised its inclusion could prejudice the beneficial effect of this kind of sympathetic block in the relief of chronic pain. Consequently, it is difficult to understand why Ruiz *et al.* used the wrong solution.

I find that hypersensitivity to the material in a variety of pharmacological agents in modified Bier's blocks has usually been revealed by a few discrete, raised, livid patches and occasionally wheals on the isolated limb. One or more similar patches or wheals may arise elsewhere on the body on release of the tourniquet; and it is at this stage that itch or discomfort arises in these cutaneous lesions wherever they are situated. It is puzzling that there was no widespread reaction upon release of the tourniquet if the reaction in the isolated limbs of the two patients reported by Ruiz *et al.* were anaphylactoid.

Could capillary damage have caused the persistent rash and discolouration in the affected limb? Both patients were elderly (aged 83 and 61) and female which would predispose them to increased capillary fragility. The authors mention that there was some oedema during the period of circulatory isolation in the treated limb of the 83-year-old

woman which surely means that extra fluid reached the limb past the tourniquet and accumulated in it. The tourniquet might not have been fully effective in this patient whose blood pressure pre-operatively was 190/100 mmHg. It is also likely that she would have had enough calcified hardening of the brachial artery to defeat the most careful tourniquet application. The injection of prilocaine 10 ml solution and a possible arterial leak past the tourniquet over 20 minutes could raise the venous pressure enough to compromise the capillaries and cause the kind of punctate, suffuse rash apparent in the illustrations of the affected limb. The tourniquet was kept inflated for 30 minutes in the other patient and here too capillary damage could have contributed to the rash.

It would have been helpful to know whether the patient had increased capillary fragility on subsequent tests. Did the authors use an automatic tourniquet and did they check the accuracy of the dial readings? It is not unusual to find

an error of this magnitude in some automatic tourniquets if they relied upon the usual method and applied 50 mmHg over the systolic pressure for the performance of a Bier's block in the upper limb. The equipment used must be stored securely after any kind of untoward clinical incident. Unused portions of the drug and stocks of the same batch number must be reserved pending further enquiries, otherwise the reputation of a valuable drug might suffer unjustly with serious consequences for the individual patient concerned and for the community at large.

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Reference

1. HANNINGTON-KIFF JG. Prilocaine for Bier's block needs methylene blue but not preservative. *Lancet* 1983; 2: 1085.

Adrenaline and anaphylaxis

Drs Alston and Oates (*Anaesthesia* 1987; 42: 892-3) reported a case of an anaphylactoid reaction during which cardiac output was measured using an Accucom cardiac output monitor. They found that cardiac output was increased during the resuscitation and as a result they advocate the use of a pure alpha-adrenergic agonist instead of adrenaline during the resuscitation of such patients. They may be correct from a purely haemodynamic point of view. However, beta-adrenergic agonists are among the most effective mast-cell stabilising agents available¹ and will inhibit further release of inflammatory mediators. Therefore, since both alpha- and beta-adrenergic agonist activities are required adrenaline remains the most logical choice despite the potential complications. The beta-adrenergic agonist activity of adrenaline also provides bronchodilatation.

Adrenaline should, therefore, be used as soon as the diagnosis of severe anaphylactoid reaction has been made.

The administration of adrenaline at this time may be both less dangerous and more effective than later in the course of the event when hypoxia, hypercarbia and acidosis may be more severe and at which time the myocardium may be more sensitive to the adverse effects of catecholamines. The incidence of adverse effects can be reduced by careful titration of the dose administered.

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Reference

1. CHURCH MK. Is inhibition of mast cell mediator release relevant to the clinical activity of anti-allergic drugs? *Agents and Actions* 1986; 18: 288-93.

Intrapleural injection

The case report about upper limb sympathetic blockade after intercostal nerve blocks by Purcell-Jones *et al.* (*Anaesthesia* 1987; 42: 284-6) was interesting. There is another explanation that is, intrapleural injection, for the spread of the block to involve the 3rd thoracic ganglion. A number of anatomical barriers inhibit extrapleural spread of local anaesthetics injected near intercostal nerves but there is little doubt that it can occur. A recent report by Kuhlman *et al.*¹ illustrates spread of large (16-29 ml) volumes of 1.5% lignocaine (with adrenaline 1:100000) up to 4 dermatomes from the site of injection. Extrapleural and paravertebral spread was demonstrated by CAT scan. However, much smaller volumes (4 ml) are unlikely to spread so extensively.

We have found that, using the method described by Reiestad², intrapleurally placed local anaesthetics can provide effective analgesia after cholecystectomy and spread is extensive. Catheters are introduced into the intrapleural space through a 17-gauge Tuohy needle and the space is usually encountered immediately after the internal intercostal membrane is breached. No information concerning the type of needle used for the blocks was given in the case report but a 22-gauge 45-degree bevel needle punctures

the pleural membrane easily once the intercostal membrane had been penetrated. Presumably the syringe containing local anaesthetic remained attached to the needle throughout, so no indication that the intrapleural space had been entered would be obtained.

It is interesting to note that our initial experiments on pig pleura (unpublished data) indicate that penetration of the parietal pleura by local anaesthetic occurs in significant amounts by 30 minutes; this is borne out by clinical observation and ties in with that noted in the report.

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References

1. KUHLMAN G, AHMAD R, CAUQUIL P, ROCHE A, EDUOARD A. Bilateral analgesia after unilateral intercostal nerve block. *Anesthesiology* 1987; 67: A284.
2. REIESTAD F, STROMSKAG KE. Intrapleural catheter in the management of postoperative pain; a preliminary report. *Regional Anesthesia* 1986; 11: 89-91.

Cardiac pacemakers and cardioplegia

We read with interest the report by Miller and Douglas (*Anaesthesia* 1987; 42: 1117) on the apparent failure of a cardioplegic solution to induce cardiac arrest in a patient with an endocardial pacemaker.

We regularly anaesthetise patients with both endocardial and epicardial pacing systems for coronary artery surgery and valve replacement. We make no specific attempt to influence the activity of the pacemaker but induce cardiac asystole with one litre of hypothermic hyperkalaemic blood cardioplegia. Electrical activity within the heart ceases in the usual manner and only returns when the aortic cross clamp is removed, which allows the pacing threshold to return to normal as residual cardioplegia is washed from the heart.

Hyperkalaemic cardioplegia induces a markedly depolarised state in the myocardial cell membrane and renders it refractory to both endogenous and exogenous electrical stimuli. Indeed, simply increasing the serum potassium concentration from 4.0 mmol/litre to 7.0 mmol/litre causes an increase in the excitability threshold from 0.5 volts to 5.05 volts.¹ The potassium concentration in our first dose of cardioplegia is approximately 20 mmol/litre with St

Thomas's solution only slightly lower than this. The Meditronic pulse generator is usually set to 5 volts. Therefore if the cardioplegia distribution is adequate it is highly unlikely that the pacemaker impulses will be propagated in the myocardium.

We suggest that the reported resistance to cardioplegia is due to inadequate cardioplegia distribution or to the potassium concentration. We do not support the recommendation that the pacemaker should be isolated prior to cardioplegia delivery. Indeed, manipulation of the pacemaker in this way may result in additional morbidity from haemodynamic instability and pouch haematoma or infection.

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Reference

1. SCOTT DL. Cardiac pacemakers as an anaesthetic problem. *Anaesthesia* 1970; 25: 87-104.

Heat and moisture exchanging bacterial filters

We believe like other workers who look after patients in the intensive care unit that there are substantial advantages in the use of heat and moisture exchanging bacterial filters in many patients who require long-term ventilation. We would, however, like to report a peculiar problem associated with their use.

In December last year we replaced the hot water bath humidifiers and heated bacteriological filters on our Servo 900B and 900C ventilators with the Pall Ultipor heat and moisture exchanging filter (BB50T). The filter was connected between the patient Y-piece and the catheter mount when in use and was changed every 24 hours as recommended by the manufacturers. Early this year we noticed that the expired minute volume meters on three of our ventilators persistently recorded inaccurately high readings. We were unable to recalibrate the expiratory flow transducers to give an accurate reading of the expired minute volume. We discovered on closer inspection of the expiratory flow transducers that the fine mesh nets of the transducers were all contaminated with inspissated material.

There was no difficulty in calibrating the expiratory flow transducers to give a correct reading of the expired minute volume when these mesh nets were replaced with new ones. All our Servo 900B and 900C ventilators are regularly serviced and the mesh nets checked and changed after every 1000 hours' use, and we have not encountered such contaminated mesh nets before.

We are uncertain as to the origin of the contaminants. It is possible that contamination could have occurred during manipulation of the equipment especially during nebulisation of drugs. We now use two Pall Ultipor filters; one in the usual location at the patient Y-piece and a second filter connected to the end of the expiratory limb just before the expiratory inlet to the ventilator to protect the machine. We change these filters after 24 hours' use and we have not had any problems since.

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A simple double lumen adapter for differential lung ventilation

Differential lung ventilation (DLV) has been suggested as a technique of ventilation in patients who have predominantly unilateral lung disease.¹ DLV has been also used to minimise shunting and optimise oxygenation in patients who undergo surgery in the lateral decubitus position.² However, the technique necessitates the simultaneous use of two anaesthesia machines and (or) two ventilators. Yamamura *et al.* have described a simple unit device for DLV for use with only one anaesthesia machine.³ The present report also describes a simple double lumen adapter which we used for DLV during thoracotomy.

The adapter has three limbs (Fig. 1). One limb of the adapter is connected to the dependent lung. The other two limbs are connected via Y-connexion to the nondependent lung; one of these limbs is provided with a stopcock which controls the tidal volume delivered to the nondependent

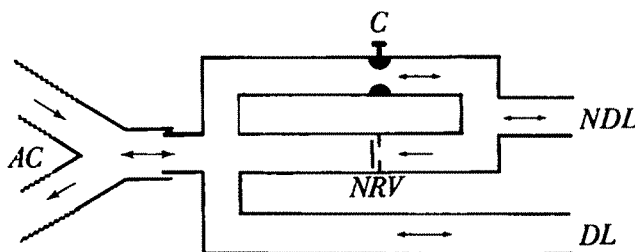


Fig. 1. A schematic diagram of the DLV adapter. The adapter is connected on one side to the Y-piece of the anaesthesia system, while the other side is connected to the double lumen tube.

lung, while the second limb is provided by a unidirectional valve which prevents flow during inflation but allows free

exhalation. The total exhaled tidal volume, as well as the tidal volume exhaled from the nondependent lung, were monitored by two Wright respirometers.

The adapter can be used for DLV during thoracotomy. It can be also utilised for DLV in patients with unilateral lung disease without the need for simultaneous use of two ventilators.

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Resistance to suxamethonium

We have read with interest the recent article by Warran *et al.* (*Anaesthesia* 1987; 42: 855-7) in which hypercholinesterasaemia was reported to be a cause of resistance to suxamethonium. They did not, however, mention the time interval between injection of the drug and the attempt at tracheal intubation. We would like to suggest a common cause of apparent resistance to suxamethonium.

We have monitored in a recent study using electromyography, the effect of suxamethonium 1 mg/kg (the dose initially used by Warran *et al.*) in 15 patients, all ASA 1 or 2. Anaesthesia was induced after a papaveretum and hyoscine premedication with thiopentone 4-5 mg/kg and fentanyl 1 µg/kg and maintained with N₂O and O₂. Additional thiopentone was given as required. Neuromuscular blockade was studied by stimulation of the ulnar nerve at the wrist with a supramaximal stimulus of 0.2 msec duration and monitoring the Evoked Compound Action Potential (ECAP) of the adductor pollicis at 15-second intervals until maximum blockade was achieved. A control value for ECAP was first established and then suxamethonium was given (1 mg/kg) preceded and followed by saline.

Time to fasciculation, block at fasciculation, maximum blockade and time to maximum blockade were measured. The results are shown in Table 1.

A block of greater than 95% was achieved in all cases but the time to maximum blockade ranged from 45 seconds to 105 seconds. Interestingly, time from onset of fasciculation to maximum block ranged from 21 secs to 72 secs. There is a tendency among anaesthetists to attempt intubation as soon as fasciculation starts. It is likely that intubation would be difficult if it is attempted at the start of fasciculation but less difficult in all patients 60 seconds later.

It is the immediacy of effect that has lead to the use of suxamethonium when a rapid sequence induction is required. Our findings confirm a widely held view that the ease of intubation in such circumstances may depend as much on the effect of the induction agent as on the muscle relaxant.

In five of these patients the termination of fasciculation was noted. Time from the end of fasciculation to maximum blockade was a mean of 38.5 seconds (range 15-50). Thus

References

- GALLAGHER TJ, BANNER MJ, SMITH RA. A simplified method of independent lung ventilation. *Critical Care Medicine* 1980; 8: 396-9.
- HEDENSTIERNA G, BAEHRENDT S, KLINGSTEDT C, SANTESSON J, SODERBERG B, DAHLBORN M, BINDSLEV L. Ventilation and perfusion of each lung during differential ventilation with selective PEEP. *Anesthesiology* 1984; 61: 369-76.
- YAMAMURA T, FURIMIDO H, SAITO Y. A single-unit device for differential lung ventilation with only one anaesthesia machine. *Anesthesia and Analgesia* 1985; 64: 1017-20.

Table 1.

Block at fasciculation (per cent)	Time to fasciculation (seconds)	Time to maximum blockade (seconds)	Maximum blockade (per cent)
75	17	45	99
94	23	45	99
3	24	45	99
16	23	60	99
43	26	60	99
19	28	60	99
3	15	75	99
27	20	75	99
25	23	75	99
49	25	75	99
5	28	75	99
72	30	75	99
91	45	75	99
34	25	90	99
48	33	105	97

resistance to suxamethonium may be due to impatience on behalf of the anaesthetist. It is not suggested that this was so in the case reported by Warran *et al.*

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R.J. CHESTNUT

A reply

Dr Chestnut's point is valid and is, I am sure, more often the explanation of difficult intubation than a high plasma cholinesterase. Our patient showed no evidence of relaxation for up to 5 minutes following the injections of suxamethonium. The complete lack of relaxation was so unusual, it prompted Dr Theeman to ask for a plasma cholinesterase estimation.

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P. WARRAN

Anaemia and Jehovah's Witness

We have one objection to the case report (*Anaesthesia* 1987; 42: 44-8) about a Jehovah's Witness who suffered from extreme acute anaemia (Hb = 1.8 g/litre on the fifth postoperative day).

The authors expected that their patient should have developed pulmonary oedema due to severe hypoproteinaemia and they argued that the application of positive end expiratory pressure ventilation might have prevented this complication. Nevertheless, they did not report the

colloid osmotic pressure (COP) of their patient. It seems unlikely that a patient, who received more than 10 litres gelatin solution with only a small volume of additional crystalloids during the first 5 days, had a severe and dangerous decrease in COP, to encourage the development of pulmonary oedema. The COP of a 5.5% gelatin solution, measured with a Knauer-Oncometer (10 000 dalton membrane) is in the range of 10.13 (SD 0.47) kPa.¹ It is more likely that the patient had an increased rather than a

decreased COP despite severe hypoproteinemia. The oedema the authors observed on hands and forearms was probably as a result of anaemic hypoxia.

Finally, we wish to add one calculation to this case report. Assuming a right-shifted oxygen dissociation curve (P_{50} 3.99 kPa) due to pre-existing anaemia,² an arterial PO_2 of 33.25 kPa with 100% HbO_2 saturation, a central venous PO_2 of 3.99 kPa, a Hb concentration of 1.8 g/100 ml and a normal oxygen uptake of 200 ml O_2 /minute this patient should have had a cardiac output of about 11 litres/minute according to Fick's law to meet her oxygen demand. Even if oxygen uptake is reduced by half (100 ml/minute), due to a decreased metabolism, cardiac output would be 5 litres/minute. It is really exceptional that this patient survived.

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References

- GRÜNERT A. *Onkometrie: Grundlagen, Meßtechnik und klinischer*

Einsatz des kolloidosmotischen Druckes. Stuttgart: Kohlhammer Verlag, 1985.

- TORRANCE J, JACOBS P, RESTREPO A, ESCHBACH J, LENFANT C, FINCH CA. Intraerythrocytic adaptation to anemia. *New England Journal of Medicine* 1970; **83**: 165-9.

A reply

We would like to thank Hasbider and colleagues for their information concerning Haemacel, and for further enlightening us in our study of this case.

When we instituted positive pressure ventilation of the lungs we did not know how much Haemacel we would use, and so used IPPV to control the anticipated pulmonary oedema. We did not advocate the use of positive end expiratory pressure ventilation.

We are grateful for their calculation of cardiac output: it would certainly have been interesting to have measured this accurately, but we considered it unjustified to put a large central line into such an anaemic patient.

It was indeed exceptional that she survived.

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P.J. HOWELL

Hypotension after guanethidine block

We read with interest the recent report by Dr Sharpe *et al.* (*Anaesthesia* 1987; **42**: 1081-3).

This is a report of a similar case. A 74-year-old woman with Ekbom's Syndrome was referred to the pain clinic for a guanethidine block to her right leg. Guanethidine 30 mg in 0.25% prilocaine 40 ml, were injected into the exsanguinated limb. A caudal epidural injection was performed at the same time with 0.125% bupivacaine 15 ml and depomedrone 40 mg. This whole procedure was performed as a day-case.

Six hours after discharge from hospital the patient was found collapsed at home with low blood pressure. She was transferred back to our hospital.

On examination in the accident and emergency department no abnormality was found apart from postural

hypotension (90/50 mmHg/supine and 75/50 mmHg/erect). A full neurological examination was normal. An electrocardiogram was also within normal limits. Her blood pressure returned to normal values 2 days later and she was discharged from hospital.

It was considered that the prolonged postural hypotension had been caused by the guanethidine. We question in view of this case, and the one reported by Dr Sharpe *et al.* whether such treatment should be carried out on a day-case basis.

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Percutaneous placement of paravertebral catheters during thoracotomy

Paravertebral local anaesthesia is a useful technique for relief of post thoracotomy pain.¹ Our experience is that attempted placement of a catheter with the method described by these authors results in a significant failure-rate due to misplacement or inability to pass the catheter.

We have found that a modification of the technique gives consistently good results. The paravertebral catheter is inserted before closure of the thoracotomy incision with the patient in the lateral position. With an aseptic technique, a 16-G Tuohy needle is inserted at 90° to the skin, 3 cm lateral to the rostral end of the vertebral spine one space cephalad of the thoracotomy incision. The needle comes into contact with the transverse process or rib of the vertebra below. A syringe of normal saline is attached to the needle which is now walked cephalad off the rib and advanced 1-1.5 cm, where loss of resistance is felt. The operator checks that a subpleural bubble of saline can be seen in the chest,

and 10 ml of saline is injected to make a space for the catheter. An end-hole catheter is inserted 5 cm through the needle and can be seen to be beneath the pleura. The Tuohy needle is removed and used to tunnel the catheter back to the mid-lane, where it is fixed in place at the end of the procedure.

We have found that 10 ml of subpleural saline and the visual check of catheter position has improved our success with this technique.

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Reference

- EASON MJ, WYATT R. Paravertebral block—a reappraisal. *Anaesthesia* 1979; **34**: 638-42.

Opisthotonos and propofol: a possible association

There have now been two reports in recent months of opisthotonos in the recovery room after general anaesthesia. Both cases involved middle-aged women having dilatation and curettage. The first was a fit, 55-year-old woman anaesthetised with droperidol, alfentanil and propofol with lignocaine. (*Anaesthesia* 1987; **42**: 565). Opisthotonos was thought to have been an extrapyramidal reaction to the droperidol. The second was an obese, 44-year-old epileptic woman given a premedication of pethidine and atropine and anaesthetised with fentanyl and propofol with lignocaine (*Anaesthesia* 1987; **42**: 1124) who also had post-operative opisthotonos and later a grand mal fit. Opisthotonos is a rare event during recovery from anaesthesia even in epileptics and a possible association with propofol was raised.

This report concerns a further case of opisthotonos, this time after induction of anaesthesia. A fit, well-built 30-year-old male with a locked knee presented for arthroscopy and meniscectomy. He had no significant medical history and was not taking any medication. He had no premedication. He was given fentanyl 0.05 mg; after five minutes he was given alfentanil 1 mg followed by propofol 200 mg given slowly. Twenty seconds after the propofol he developed marked opisthotonos with his back and neck arched, his arms extended, eyes looking upwards, and pupils widely dilated. This lasted 15 seconds. Then he relaxed spontaneously. Pulse and blood pressure remained satisfactory. His trachea was then intubated (without relaxant). Regular breathing resumed after 10 minutes and he then breathed nitrous oxide, oxygen and isoflurane spontaneously for 1.25 hours. The remainder of the anaesthetic was unremarkable as was the recovery.

Excitatory phenomena on induction of anaesthesia are generally minimal after propofol and significantly less than after etomidate or methohexitone.¹ However, epileptiform movements are known to occur and have recently been added to the data sheet.

Pretreatment with fentanyl is known to increase blood levels of propofol by 50%.² However, this interaction is not thought to occur between alfentanil and propofol.³ Whether opisthotonos relates solely to the use of propofol or only occurs after pretreatment with fentanyl or alfentanil has yet to be determined. The manufacturers are only aware of one other recent report of opisthotonos. This occurred after induction of anaesthesia with fentanyl and propofol in an 11-year-old girl.³ Opisthotonos is obviously extremely rare. However, its possible association with fentanyl or alfentanil and propofol should now be considered.

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References

1. WELLS JKG. Comparison of ICI 35868, etomidate and methohexitone for day case anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 732-5.
2. COCKSHOTT ID, BRIGGS LP, DOUGLAS EJ, WHITE M. Pharmacokinetics of propofol in female patients. *British Journal of Anaesthesia* 1987; **59**: 1103-10.
3. ICI. Pharmaceutical Information Service. *Personal communication* 1987.

An unusual case of upper airways obstruction

An 18-month-old child was admitted after a fall whilst running with a spoon in his mouth. The spoon became impacted with the handle protruding from the mouth. Attempts by the parents to remove it had proved impossible.

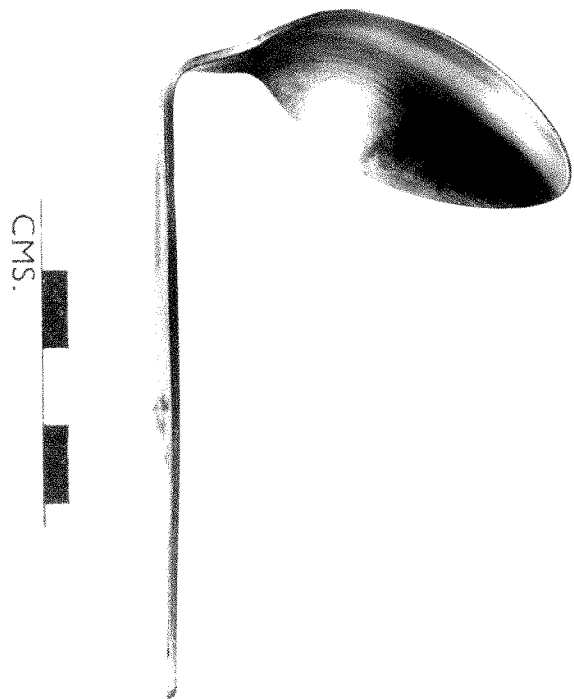
On arrival he had marked upper airways obstruction with inspiratory stridor complicated by copious salivation, vomiting and slight bleeding. Direct visualisation was impossible and any attempt to remove the spoon produced complete upper airways obstruction and cyanosis. X rays, taken before anaesthetic assistance had been sought, showed the tip of the spoon in the nasopharynx and the handle bent through 90° protruding through the mouth.

He was immediately taken to theatre where intravenous access was secured. Atropine 10 µg/kg was given intravenously which led to a marked clinical improvement and reduction of salivation before the arrival of the ENT surgeon.

The degree of soft tissue damage was unknown. The X rays did not help in the assessment but it was considered that there might be much soft tissue swelling and bleeding when the spoon was removed.

An inhalation induction with oxygen and halothane was performed with the child head down in the left lateral position. An elective tracheostomy was performed and the airway secured. The spoon was tightly impacted but eventually removed (Fig. 1). There was no soft tissue damage except a small uvular tear which did not bleed. The patient was recovered uneventfully in the intensive therapy unit and the tracheostomy was removed 14 hours after the procedure.

This unusual case confirms that X rays, apart from their ability to illustrate the problem, are clinically of little help



in this situation. They are also potentially dangerous. We found the antisialogogue action of atropine very helpful in the management of the airway before surgery.

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M. PRICE

Unrecognised dural punctures

We note with interest that of the 21 unintentional dural punctures reported by Drs Okell and Sprigge, (*Anaesthesia* 1987; 42: 1110-3), one third were not recognised at the time of the epidural and were discovered when the patients developed typical spinal headaches in the postpartum period. This is consistent with our own experience,¹ where of 19 patients who required blood patch, 6 dural taps had not been recognised at the time of the epidural puncture. This emphasises the need for improvement in our means of detection of the dural tap.

Drs Okell and Sprigge do not report if more than one attempt had been made at the epidural puncture in their unrecognised dural taps, which was the case with all 6 of ours. Our suggestion that the dural tap occurs during the unsuccessful attempt is a more likely occurrence than the mechanisms they have postulated.

An epidural top-up through a subsequently successfully placed catheter after a dural tap rarely produces an extensive block, since the pressure gradients do not favour the migration of local anaesthetic through the dural hole. It is not surprising, therefore, that these unrecognised dural taps were not revealed by the test dose. However, they may have been revealed by the physical test previously described.^{2,3} We suggest the routine use of this test prior to any pharmacological ones to reduce the incidence of unrecognised dural taps. We also reiterate our earlier recommendation to withdraw the needle very slowly, with the stylette removed, whenever an attempt to enter the epidural space has failed.

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References

1. SHAH JL, VENESS AM. Epidural blood patch using a catheter. Diagnosis of an unrecognised dural tap. *Anaesthesia* 1985; 40: 1120-3.
2. SHAH JL. A test to show correct placement of epidural catheter. *Anaesthesia* 1982; 37: 426-7.
3. SHAH JL. Epidural test doses in obstetrics. *Anaesthesia* 1985; 40: 1131.

In their survey (*Anaesthesia* 1987; 42: 1110-3), Drs Okell and Sprigge say that fluid dripping from a Tuohy needle may cause confusion if loss of resistance to saline is used to identify the epidural space. Such dripping could be due to dural puncture or to saline in the epidural space at greater than atmospheric pressure. I have made some measurements in anaesthetised, nonpregnant adults, which suggest that the rate and duration of any reflux gives a strong indication of its cause. Using a 16-gauge Tuohy needle, I injected 10 ml aliquots of saline into the epidural space of eight subjects, and measured epidural pressure and reflux over a 15-sec period after each injection. Reflux at pressures of 0.2-5.0 kPa was measured; this range represents that measured in labouring women.¹ The highest recorded reflux rate was

surprisingly low, only one drop every two seconds. At the end of the tests, when pressure was highest, reflux was allowed to continue in an attempt to recover the saline. In all cases the flow reduced rapidly and stopped within one minute. A dural puncture would give far more rapid reflux than this. Such low flows might occur if a small part of the needle bevel entered the subarachnoid space but in this circumstance the flow would continue as long as the needle remained in this position.

These findings may not apply to conscious patients in labour, but I suggest that anyone who uses saline to identify the epidural space and who notices fluid reflux from a 16-gauge Tuohy needle should only suspect a dural puncture in the presence of persistent reflux greater than one drop every two seconds.

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Reference

1. GALBERT MW, MARX GF. Extradural pressures in the parturient patient. *Anesthesiology* 1974; 40: 499-502.

A reply

We are grateful for the opportunity to reply to the letters of Drs Veness and Shah and Dr Coe. We are interested to learn that Veness and Shah report a similar incidence of dural puncture, not recognised at the time, but which presented as postpartum headache.

No difficulty was experienced in the procedure in five out of seven cases and the patients behaved normally apart from the headaches that developed later.

We were interested to read about Dr Shah's test. We suspect that in these five cases it would have been negative since we believe that the catheter was placed correctly in the epidural space. In the remaining two cases, and in two other cases in which the catheter appeared to have entered the subarachnoid space, Dr Shah's test would have been useful and Dr Coe's observation on the different rates of efflux of fluid from an epidural needle, for saline or CSF, is interesting.

One of the conclusions that we drew from our observations on accidental dural puncture was that Murphy's law should be respected. If anything can go wrong it may do sometimes. An epidural catheter is inserted blindly and it may be misplaced either wholly or partially, for example into the subarachnoid space or into an epidural vein. This misplacement may go undetected despite tests. Therefore we give epidural doses as small increments so that if misplacement has occurred it may be suspected before a large dose of the drug has been injected into the wrong place.

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Tracheal tubes for neuroanaesthesia

In the light of recent controversy over the use of armoured tubes for neuroanaesthesia, I thought it would be useful to present information which reflects current practice within the United Kingdom.

A random sample taken in 1986 of tracheal tube use from 27 neurosurgical units is given in Table 1. There was a

strong preference for armoured tubes for neurosurgical procedures, regardless of the position of the patient. Interestingly, half of the tubes used by these anaesthetists were made of polyvinyl chloride (PVC). This suggests a trend away from the latex rubber tubes which have recently been shown to be unsafe if used repeatedly.¹ Approximately

Table 1. Percentage of tracheal tube types used for neurosurgery and neuroradiology

Type of tube	Neurosurgery		Neuroradiology	
	Supine	Prone	Angiography	CT Scan
Armoured latex	37	40	23	17
Oxford	3	3	7	7
PVC	23	20	60	73
Armoured PVC	37	37	10	3

20 per cent of the respondents used non armoured PVC tubes, again, regardless of the position of the patient. This, although a minority, supports the view expressed earlier that non armoured PVC tubes may be safely used for neurosurgery.^{2,3} Finally, although nearly one third of patients undergoing angiography received an armoured tube, there was an overall preference for plain PVC tracheal tubes for

diagnostic neuroradiology. Now that cerebral angiography is almost always performed via the femoral route, is there really any indication for the use of armoured tubes during diagnostic procedures in the supine position?

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References

1. WRIGHT PJ, MUNDY JVB. Tracheal tubes in neuroanaesthesia. Nylon reinforced latex rubber tracheal tubes. *Anaesthesia* 1987; **42**: 1012-4.
2. WRIGHT PJ. Are armoured tubes really necessary for neuroanaesthesia? *Anaesthesia* 1986; **47**: 213.
3. BRISTOW ASE. Armoured tubes for neuroanaesthesia. *Anaesthesia* 1986; **41**: 776.

Modification of coaxial breathing system

It was interesting to read the letter by Dr P.J. Roberts, (*Anaesthesia* 1987; **72**: 1128) about a modification of the coaxial breathing system by freeing the distal end of inner tube since I suggested the same modification seven years ago.¹

Mr R. Sugg of Penlon made this modification but after large scale trials it was found that a potential hazard existed since the free inner tube could enter and obstruct the tracheal tube connexion. It was difficult to control the relative lengths of inner and outer tubes with sufficient accuracy to prevent this hazard. Penlon are now reviewing the situation

and in the light of new and better manufacturing techniques this problem could be eliminated.

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Reference

- ¹ NAQVI NH. Torsion of inner tube. *British Journal of Anaesthesia* 1981; **53**: 193.

Kinking of the pilot tube

Drs Tanski and James (*Anaesthesia* 1986; **41**: 1060) described an incident when kinking of the pilot tube at its take-off prevented the deflation of the tracheal tube cuff at extubation. Our department has recently changed from red rubber to disposable PVC tracheal tubes and I have experienced similar problems including some variations. It proved impossible in one case to add a further small aliquot of air to the cuff to effect a total seal because the pilot tube had been kinked at its take-off by the securing ribbon gauze. The tracheal tube cuff in a second case was found to have deflated about 5 minutes after intubation. Close examination revealed that the pilot tube had again been kinked

at its take-off and as a result had split. It was impossible to maintain inflation of the cuff so the tube was changed. The first example involved Mallinckrodt Lo-pro tube and the latter a Franklin Sensiv.

These problems are undoubtedly a result of the high take-off of the pilot tube in both products as pointed out by Drs Tanski and James, but a secondary factor is the low visibility of the transparent PVC pilot tube compared to the garish colour of the red rubber version.

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Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for November 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

- Effects of upper or lower abdominal surgery on diaphragmatic function. CANTINEAU JP, DESMONTS JM. *British Journal of Anaesthesia* 1987; **59**: 1230.
- Myogenic electrical control activity in longitudinal muscle of human and dog colon. CHOW E, HUIZINGA JD. *Journal of Physiology* 1987; **392**: 21.
- Effect of somatostatin analog on water and electrolyte transport and transit time in human small bowel. DUENO MI, BAI JC *et al.* *Digestive Diseases and Sciences* 1987; **32**: 1092.
- Focal gastric mucosal blood flow by laser-Doppler and hydrogen gas clearance: a comparative study. GANA TJ, HUHLEWYCH R, KOO J. *Journal of Surgical Research* 1987; **43**: 337.
- Vago-vagal activation of naloxone-sensitive non-adrenergic, non-cholinergic jejunal contractions in anaesthetized cat. GUSTAFSSON B, DELBRO D. *Acta Physiologica Scandinavica* 1987; **131**: 19.
- Splenic blood flow measurements by Doppler ultrasound—a preliminary report: MANOHARAN A, GILL RW, GRIFFITHS KA. *Cardiovascular Research* 1987; **21**: 779.
- Warfarin inhibition of metastasis: the role of anticoagulation. McCULLOCH PM, GEORGE WD. *British Journal of Surgery* 1987; **74**: 879.
- Effects of acetylcholine and atropine, respectively, on spontaneous contractions of the isolated colonic circular smooth muscle in the rat. NILSSON L, FASTH G *et al.* *Acta Physiologica Scandinavica* 1987; **131**: 155.
- Mechanism of 'substance P': on mesenteric blood flow; interactions with opioid peptides. ROZSA Z, VARRO V. *Neuropeptides* 1987; **10**: 275.
- The effect of weight loss, operation and parenteral nutrition on fat clearance in patients with colorectal cancer. WILSON AW, KIRK CJC, GOODE AW. *Clinical Science* 1987; **73**: 497.

Pharmacology

Adrenergic drugs and their antagonists

- The effect of twice daily nadolol on intraocular pressure. DUFF GR. *American Journal of Ophthalmology* 1987; **104**: 343.
- Long-term effects of beta-adrenergic blockade with nadolol on hepatic and renal haemodynamics and function in cirrhotics. GATTA A, BOLOGNESI M *et al.* *Clinical Physiology* 1987; **7**: 377.
- Clonidine-induced suppression of plasma catecholamines in states of adrenal medulla hyperfunction. GROSS MD, SHAPIRO B *et al.* *Journal of Endocrinological Investigation* 1987; **10**: 359.
- Binding in vitro of piprenaline on to plasma proteins and blood cells in man. HAUSSINGER D, BRODDE O-E, STARKE K. *Biochemical Pharmacology* 1987; **36**: 3509.
- Clonidine: understanding its disposition, sites and mechanism of action. JARROTT B, CONWAY EL *et al.* *Clinical and Experimental Pharmacology and Physiology* 1987; **14**: 471.
- Effects of beta 1 and beta 1 + beta 2-antagonists on training-induced myocardial hypertrophy and enzyme adaptation. Ji LL, STRATMAN FW, LARDY HA. *Biochemical Pharmacology* 1987; **36**: 3411.

- Human vascular alpha-adrenoreceptors: The relevance of subtypes. MOULDS RFW, STEVENS MJ, JENKIN RA. *Clinical and Experimental Pharmacology and Physiology* 1987; **14**: 379.
- Adrenoceptor classification. RAPER C. *Clinical and Experimental Pharmacology and Physiology* 1987; **14**: 401.

Anaesthetic agents

- Halothane metabolism in cirrhotic rats. BADEN JM, SERRA M *et al.* *Anesthesiology* 1987; **67**: 660.
- Psychological effect of detailed preanesthetic information. ELSASS P, EIKARD B *et al.* *Acta Anaesthesiologica Scandinavica* 1987; **31**: 579.
- General anesthesia and hepatic circulation. GELMAN S. *Canadian Journal of Physiology and Pharmacology* 1987; **65**: 1762.
- Trichloroethylene and halothane inhibit uptake and metabolism of 5-hydroxytryptamine in rat lung slices. RAGNAR HA, BERGLUND BG, POST C. *Pharmacology & Toxicology* 1987; **61**: 191.
- Anesthetic depression of myocardial contractility: a review of possible mechanisms. RUSY BF, KOMAI H. *Anesthesiology* 1987; **67**: 745.
- Antibody to halothane-induced liver antigen. SPENCE AA. *British Journal of Anaesthesia* 1987; **59**: 1202.
- Cardiopulmonary function during 7 h of constant-dose halothane and methoxyflurane. STEFFEY EP, FARVER TB, WOLNER MJ. *Journal of Applied Physiology* 1987; **63**: 1351.
- Effects of intravenous atropine on static P-V curves of the lung in normal man. TERRA-FILHO J, MANCO JC *et al.* *Respiration Physiology* 1987; **70**: 265.
- Actions of halothane on the electrical activity of Purkinje fibers derived from normal and infarcted canine hearts. TURNER LA, BOSNIAC ZJ, KAMPINE JP. *Anesthesiology* 1987; **67**: 619.
- Methohexital activation of epileptogenic foci during acute electrocorticography. WYLER AR, RICHEY ET *et al.* *Epilepsia* 1987; **28**: 490.
- Hypotensive effect of naloxone on high blood pressure induced by stress in the rat. FLORENTINO A, JIMENEZ I *et al.* *Life Sciences* 1987; **41**: 2445.
- The pharmacokinetics of alfentanil in children. GORESKY GV, KOREN G *et al.* *Anesthesiology* 1987; **67**: 654.
- First pass uptake of fentanyl, meperidine, and morphine in the human lung. ROERIG DL, KOTRLY KJ *et al.* *Anesthesiology* 1987; **67**: 466.
- Psychomotor, respiratory and neuroendocrinological effects of buprenorphine and amitriptyline in healthy volunteers. SAARIALHO-KERE U, MATTILA MJ *et al.* *European Journal of Clinical Pharmacology* 1987; **33**: 139.
- Tolerance to morphine microinjections in the periaqueductal gray (PAG) induces tolerance to systemic, but not intrathecal morphine. SIUCIAK JA, ADVOKAT C. *Brain Research* 1987; **424**: 311.

Muscle relaxants

- Influence of priming on the potency of non-depolarizing neuromuscular blocking agents. BRADY MM, MIRAKHUR RK, GIBSON FM. *British Journal of Anaesthesia* 1987; **59**: 1245.

- Continuous infusion of vecuronium: The effect of anesthetic agents. CANNON JE, FAHEY MR. *Anesthesiology* 1987; **67**: 503.
- Blockade and recovery of cholinergic transmission in rats treated with hemicholinium 3. CARPENTER FG, WOODRUFF CR. *European Journal of Pharmacology* 1987; **141**: 179.
- Dantrolene and mepacrine antagonize the hemolysis of human red blood cells by halothane and bee venom phospholipase A2. FLETCHER JE, KISTLER P *et al.* *Toxicology and Applied Pharmacology* 1987; **90**: 410.
- Pharmacokinetics and pharmacodynamics of vecuronium administered by bolus and infusion during halothane or balanced anesthesia. SHANKS CA, AVRAM MJ *et al.* *Clinical Pharmacology & Therapeutics* 1987; **42**: 459.
- The effects of succinylcholine on mouth opening. VAND DER SPEK AFL, FANG WB *et al.* *Anesthesiology* 1987; **67**: 459.

Other drugs

- Effects of concurrent sucralfate administration on pharmacokinetics of naproxen. CAILLE G, DU SOUICH *et al.* *American Journal of Medicine* 1987; **83**: 67.
- Metabolic n-oxidation of metronidazole. ESSIEN EE, OGONOR II *et al.* *Journal of Pharmacy and Pharmacology* 1987; **39**: 843.
- Life-threatening water intoxication during somatostatin therapy. HALMA C, JANSEN JBMJ *et al.* *Annals of Internal Medicine* 1987; **107**: 518.
- The mechanism of the warfarin/rifampin drug interaction in humans. HEIMARK LD, GIBALDI M *et al.* *Clinical Pharmacology & Therapeutics* 1987; **42**: 388.
- Cross reverse tolerance between amphetamine, cocaine and morphine. HUIKURO K, KANETO H. *Journal of Pharmacobio-Dynamics* 1987; **10**: 503.
- Endogenous nitric oxide inhibits human platelet adhesion to vascular endothelium. RADOMSKI MW, PALMER RMJ, MONCADA S. *Lancet* 1987; **2**: 1057.
- Aging and drug disposition. SCHMUCKER DL, LONERGAN ET. In: BABIGHIAN G, ed., *Otology today*. (Basel): S Karger, 1987 509.
- Clinical efficacy of sucralfate in reflux esophagitis: comparison with cimetidine. TYTGAT GN. *American Journal of Medicine* 1987; **83**: 38.
- Pharmacokinetics of rimantadine hydrochloride in patients with chronic liver disease. WILLS RJ, BELSHE R *et al.* *Clinical Pharmacology & Therapeutics* 1987; **42**: 449.

Apparatus

- Indirect blood pressure monitoring in the postpartum patient. KIRSHON B, LEE W *et al.* *Obstetrics and Gynecology* 1987; **70**: 799.
- Estimation of oxygen utilization by dual oximetry. RASANEN J, DOWNS JB *et al.* *Annals of Surgery* 1987; **206**: 621.

Complications

- Pulmonary artery false aneurysms secondary to Swan-Ganz pulmonary artery catheters. DIEDEN JD, FRILOUX LA, RENNER JW. *American Journal of Roentgenology* 1987; **149**: 901.
- Cerebral vasculitis associated with cocaine abuse. KAYE BR, FAINSTAT M. *Journal of the American Medical Association* 1987; **258**: 2104.
- Acute renal failure and multiple organ system failure. SHEN PF, ZHANG S. *Archives of Surgery* 1987; **122**: 1131.

General anaesthetic procedures

- Anaesthesia for trans-sternal thymectomy in myasthenia gravis. REDFERN N, MCQUILLAN PJ *et al.* *Annals of The Royal College of Surgeons of England* 1987; **69**: 289.
- Operations postponed by anaesthetists: a prospective study. WHELAN E, GORDON HL. *Annals of The Royal College of Surgeons of England* 1987; **69**: 296.

General interest

- Usefulness of basal catecholamine plasma levels and clonidine suppression test in the diagnosis of pheochromocytoma. MAN-

- NELLI M, DE FEO ML *et al.* *Journal of Endocrinological Investigation* 1987; **10**: 377.
- A case of recurrent malignant pheochromocytoma complicated by the watery diarrhea, hypokalemia, achlorhydria syndrome. NIGAWARA K, SUZUKI T *et al.* *Journal of Clinical Endocrinology & Metabolism* 1987; **65**: 1053.
- Pre-operative assessment of fitness score. PLAYFORTH MJ, SMITH GMR *et al.* *British Journal of Surgery* 1987; **74**: 890.
- Current concepts—T lymphocytes: ontogeny, function, and relevance to clinical disorders. ROYER HD, REINHERZ EL. *New England Journal of Medicine* 1987; **317**: 1136.
- Some aspects of the biology of nitrogen-fixing organisms. SPRENT JI, SUTHERLAND JM, DE FARIA SM. *Philosophical Transactions of The Royal Society of London* 1987; **317**: 111.

Spinal and epidural analgesia

- Use of Mu & delta opioid peptides of various selectivity gives further evidence of specific involvement of Mu opioid receptors in supraspinal analgesia DAUGE V, PETIT F *et al.* *European Journal of Pharmacology* 1987; **141**: 171.

Spinal opioids

- Long term intrathecal administration of morphine: a comparison of bolus injection via reservoir with continuous infusion by implanted pump. BRAZENOR GA. *Neurosurgery* 1987; **21**: 484.
- U-opiate binding and morphine antagonism by octapeptide analogs of somatostatin. WALKER JM, BOWEN WD *et al.* *Peptides* 1987; **8**: 869.

Obstetric anaesthesia and analgesia

- Myometrial desensitization after ritodrine infusion. CARITIS SN, CHIAO JP *et al.* *American Journal of Physiology* 1987; **253** (Part 2): E410.
- Oxytocin during labor after previous cesarean section—results of a multicenter study. FLAMM BL, GOINGS JR *et al.* *Obstetrics and Gynecology* 1987; **70**: 709.
- Effect of epidural analgesia with bupivacaine hydrochloride on neonatal bilirubin production. GALE R, FERGUSON JE, STEVENSON DK. *Obstetrics and Gynecology* 1987; **70**: 692.
- Effects of extradural anaesthesia on human fetal blood flow in-utero—comparison of 3 local anaesthetic solutions. LINDBLAD A, BERNOW J *et al.* *British Journal of Anaesthesia* 1987; **59**: 1265.
- Maternal and neonatal outcome in pregnancies with no risk factors. MOUTQUIN JM, GAGNON R *et al.* *Canadian Medical Association Journal* 1987; **137**: 728.
- The continuous measurement of transcutaneous carbon dioxide tension (TcPCO₂), an atraumatic tool to verify fetal acidosis? SCHMIDT SCH, SALING EZ. *British Journal of Obstetrics and Gynaecology* 1987; **94**: 963.
- Emergency requirements of pregnancy in the Netherlands. VAN RAAL JM, VERMAAT-MIEDEMA SH *et al.* *Lancet* 1987; **2**: 953.

Paediatric anaesthesia and intensive care

- Persistent fetal pulmonary hypoperfusion after acute hypoxia. ABMAN SH, ACCURSO FJ *et al.* *American Journal of Physiology* 1987; **253** (Part 2): H941.
- Respiratory gases, acid-base balance and lactate concentrations of the midterm human fetus. BOZZETTI P, BUSCAGLIA M *et al.* *Biology of the Neonate* 1987; **52**: 188.
- Role of catecholamines in mediating fetal blood volume decrease during acute hypoxia. BRACE RA, CHEUNG CY. *American Journal of Physiology* 1987; **253** (Part 2): H927.
- Effects of chronic hypoxia from birth on the ventilatory response to acute hypoxia in the newborn rat. EDEN GJ, HANSON MA. *Journal of Physiology* 1987; **392**: 11.
- Maturation of the respiratory response to acute hypoxia in the new born rat. EDEN GJ, HANSON MA. *Journal of Physiology* 1987; **392**: 1.
- High frequency ventilation in the neonatal period. GREENOUGH A, MILNER AD. *Archives of Disease in Childhood* 1987; **62**: 446.
- Failure of autoregulation of cerebral blood flow in neonates studied by pulsed doppler ultrasound of the internal carotid

- artery. JORCH G, JORCH N. *Archives of Disease in Childhood* 1987; **62**: 468.
- The pharmacokinetics of naloxone in the premature newborn. LEE STILE I, FORT M *et al. Developmental Pharmacology and Therapeutics* 1987; **10**: 454.
- Glucose utilization by the placenta of anesthetized rats: Effect of insulin, glucose, and ketone bodies. LETURQUE A, HAUGUEL S *et al. Pediatric Research* 1987; **22**: 483.
- Serum protein binding of furosemide in newborn infants and children. PACIFICI GM, VIANI A, TADDEUCCI-BRUNELLI G. *Developmental Pharmacology & Therapeutics* 1987; **10**: 413.
- Effect of fetal adrenalectomy on catecholamine release and physiologic adaptation at birth in sheep. PADBURY J, AGATA Y *et al. Journal of Clinical Investigation* 1987; **80**: 1096.

Cardiovascular system

Physiology

- Hypercoagulability: a conceptual and diagnostic approach. ANSELL JE. *American Heart Journal* 1987; **114** (Part 1): 910.
- Neurotoxins that act selectively on voltage-dependent cardiac calcium channels. BROWN AM, YATANI A *et al. Circulation Research* 1987; **61** (Suppl): 1-6.
- The responses of atrial natriuretic factor concentrations to acute volume changes in conscious rats. CHIU PJS, VEMULAPALLI S *et al. Life Sciences* 1987; **41**: 2339.
- Paradoxical inhibition of atrial natriuretic peptide release during pacing-induced hypotension. ERNE P, RAINE AEG, *et al. Clinical Science* 1987; **73**: 459.
- Structure and function of the arteries in hypertension. FOLKOW B. *American Heart Journal* 1987; **114** (Part 2): 938.
- Responses of vasopressin and enkephalins to hemorrhage in adrenalectomized dogs. INOUE M, KIMURA T *et al. American Journal of Physiology* 1987; **253** (Part 2): R467.
- Blood pressure regulation, peripheral renin activity and aldosterone in patients with pyelonephritic renal scarring. JACOBSON SH. *Acta Physiologica Scandinavica* 1987; **131** (No. 2): 242.
- Endorphinergic mechanism in the central cardiovascular and analgesic effects of clonidine. KUNOS G, MOSQUEDA-GARCIA R *et al. Canadian Journal of Physiology and Pharmacology* 1987; **65**: 1624.
- Physiological balance of haemostasis and bleeding. MARDER VJ, FRANCIS CW. *Drugs* 1987; **33**: 13.
- Diastolic time in congestive heart failure. MEILER SEL, BOUDOUHAS H *et al. American Heart Journal* 1987; **114**: 1192.
- Atrial natriuretic peptides in man. NICHOLLS MG, IKRAM H *et al. Canadian Journal of Physiology & Pharmacology* 1987; **65**: 1697.
- Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to graded hemorrhage. PEREL A, PIZOV R, COTEV S. *Anesthesiology* 1987; **67**: 498.
- Mechanisms for the release of atrial natriuretic peptide. RANKIN AJ. *Canadian Journal of Physiology and Pharmacology* 1987; **65**: 1673.
- Diurnal change in plasma atrial natriuretic peptide concentrations. RICHARDS AM, TONOLO G *et al. Clinical Science* 1987; **73**: 489.
- Acute myocardial infarction: Measurement of arachidonate end-products in whole blood as an index of platelet cyclo-oxygenase activity in vivo. ROUSSON D, LAGARDE M *et al. Thrombosis Research* 1987; **48**: 63.
- Human cardiovascular adjustments to acute hypoxaemia. ROWELL LB, BLACKMON JR. *Clinical Physiology* 1987; **7**: 349.
- Review: von Willebrand factor and von Willebrand disease. RUGGERI ZM, ZIMMERMAN S. *Blood* 1987; **70**: 895.
- Central opioid mechanisms and cardiovascular control in hemorrhagic hypotension. SANDOR P, DE JONG W *et al. American Journal of Physiology* 1987; **253** (Part 2): H507.
- Central venous pressure—a physiological stimulus for secretion of atrial natriuretic peptide in humans? SCHUTTEN HJ, JOHANNESEN AC *et al. Acta Physiologica Scandinavica* 1987; **131**: 265.
- Hemodynamic and hormonal effects of atrial natriuretic factor in patients with essential hypertension. VOLPE M, MELE AF *et al. Journal of the American College of Cardiology* 1987; **10**: 787.
- Superoxide dismutase in rats with sepsis: effect on survival rate and amino acid transport. WARNER BW, HASSEIGREN P *et al. Archives of Surgery* 1987; **122**: 1142.
- Spasticity and drug therapy. WUIS EW. *Pharmaceutisch Weekblad* 1987; **9**: 249.
- Treatment and medication**
- Possible role of oxygen-derived, free radicals in cardiocirculatory shock. BORMAN KR. *Surgery Gynecology & Obstetrics* 1987; **165**: 293.
- Acute and chronic hemodynamic effects of nicardipine hydrochloride in patients with heart failure. BURLEW BS, GHBORGHIADE M *et al. American Heart Journal* 1987; **114** (Part 1): 793.
- The trans-hepatic extraction of nifedipine. CHALLENGER VF, WALLER DG *et al. British Journal of Clinical Pharmacology* 1987; **24**: 473.
- Calcium channel blocker drugs and diabetic control. COLLINS WCJ, CULLEN MJ, FEELY J. *Clinical Pharmacology & Therapeutics* 1987; **42**: 420.
- Beta-adrenergic inotropic responsiveness of patients with heart failure: studies with intracoronary dobutamine infusion. COLUCCI WS, LEATHERMAN GF *et al. Circulation Research* 1987; **61** (Suppl): 1-82.
- Survival from cardiac arrest in the accident and emergency department. COPE AR, QUINTON DN *et al. Journal of The Royal Society of Medicine* 1987; **80**: 746.
- Control of hypertension in elderly patients with felodipine and metoprolol: a double-blind, placebo-controlled in clinical trial. FEELING P, DAVIS RH *et al. British Journal of Clinical Pharmacology* 1987; **24**: 459.
- Dipyridamole: pharmacokinetics and effects on aspects of platelet function in man. GREGOV D, JENKINS A *et al. British Journal of Clinical Pharmacology* 1987; **24**: 425.
- Oxygenation of cardioplegic solutions—potential for the calcium paradox. HENDREN WG, GEFFIN GA *et al. Journal of Thoracic and Cardiovascular Surgery* 1987; **94**: 614.
- Early cardiovascular changes with ibopamine: evidence for a biphasic haemodynamic action. HOGG KJ, HORNUNG RS *et al. British Journal of Clinical Pharmacology* 1987; **24**: 435.
- Cardiovascular depression by verapamil: reversal by glucagon and interactions with propranolol. JOLLY SR, KIPNIS JN, LUCCHESI BR. *Pharmacology* 1987; **35**: 249.
- Transfusion medicine. KLEIN HG. *Journal of American Medical Association* 1987; **258**: 2108.
- Evaluation of left ventricular diastolic function: clinical relevance and recent doppler echocardiographic insights. LABOVITZ AJ, PEARSON AC. *American Heart Journal* 1987; **114** (Part 1): 836.
- Effect of naloxone on regional cerebral blood flow during endotoxin shock in conscious rats. LAW WR, FERGUSON JL. *American Journal of Physiology* 1987; **253** (Part 2): R425.
- Controlled reperfusion following regional ischemia. LAZAR HL, WEI J *et al. Annals of Thoracic Surgery* 1987; **44**: 350.
- The role of drugs in countering adverse pathophysiological profiles: influence on hemodynamics. LUND-JOHANSEN P. *American Heart Journal* 1987; **114** (Part 2): 958.
- Supraventricular tachycardia. MANOLIS AS, ESTES NAM. *Archives of Internal Medicine* 1987; **147**: 1706.
- Pharmacologic approaches to management of arrhythmias in patients with cardiomyopathy and heart failure. MYERBURG RJ, KESSLER KM *et al. American Heart Journal* 1987; **114**: 1273.
- Effect of beta-adrenergic receptor blockade on atrial natriuretic peptide in essential hypertension. NAKAOKA H, KITAHARA Y *et al. Hypertension* 1987; **10**: 221.
- Choice of antihypertensive drug therapy. PRITCHARD BNC, TOMLINSON B. *American Heart Journal* 1987; **114** (Part 2): 1030.
- Celiprolol: a preliminary review of its pharmacodynamic and pharmacokinetic properties and its therapeutic use in hypertension and angina pectoris. RIDDELL JG, SHANKS RG, BROGDEN RN. *Drugs* 1987; **34**: 438.
- Hyperosmotic sodium salts reverse severe hemorrhagic shock: other solutes do not. ROCHA E SILVA M, VELASCO IT *et al. American Journal of Physiology* 1987; **253** (Part 2): H751.
- Echocardiographic prediction of postoperative low cardiac output syndrome in patients with mitral stenosis. SANO S, NAWA S *et al. Acta Medica Okayama* 1987; **41**: 215.
- Blood substitution and complement activation. SCHATT U, BERSHUS O, JAREMO J. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 559.
- Nonpharmacologic treatment of life-threatening cardiac arrhythmias. SCHEINMAN MM. *American Heart Journal* 1987; **114**: 1291.
- Encainide: A new and potent antiarrhythmic. SOMBERG JC, ZNGER D *et al. American Heart Journal* 1987; **114** (Part 1): 826.

- The ability of oxygenated fluorocarbon solution to minimize ischemic skeletal muscle injury. TAKAHASHI F, TSAI TM *et al. Plastic and Reconstructive Surgery* 1987; **80**: 582.
- Decreased renal perfusion after correction of experimental coarctation. TARKKA M, UHARI M *et al. Pediatric Research* 1987; **22**: 445.
- Prognosis after cardiac arrest due to ventricular tachycardia or ventricular fibrillation associated with acute myocardial infarction. TOFLER GH, STONE PH *et al. American Journal of Cardiology* 1987; **60**: 755.
- Pharmacokinetics and pharmacodynamics of antiarrhythmic agents in patients with congestive heart failure. WOOSLEY RL. *American Heart Journal* 1987; **114**: 1280.

Respiration

Physiology

- Influence of extreme hypercapnia on respiratory motor nerve activity in cats. BARTLETT D, KNUTH SL, WARD DK. *Respiration Physiology* 1987; **70**: 173.
- Effect of posture on ventilation and breathing pattern during room air breathing at rest. BAYDUR A, BEHRASIS PK *et al. Lung* 1987; **165**: 341.
- Pulmonary microembolism: a cause of lung injury. BEAL SL, REED RL II. *Journal of Surgical Research* 1987; **43**: 303.
- Assessment of exercise oxygen consumption as preoperative criterion for lung resection. BECHARD D, WEISTEIN L. *Annals of Thoracic Surgery* 1987; **44**: 344.
- Oxygen radicals and human disease. CROSS CE, HALLIWELL B *et al. Annals of Internal Medicine* 1987; **107**: 526.
- Leukotrienes and airway responses. DRAZEN JM, AUSTEN KF. *American Review of Respiratory Diseases* 1987; **136**: 985.
- Nasal continuous positive airway pressure in atelectasis. DUNCAN SR, NEGRIN RS *et al. Chest* 1987; **92**: 621.
- Nocturnal oxyhemoglobin desaturation in COPD patients with arterial oxygen tensions above 60 mmHg. FLETCHER EC, MILLER J *et al. Chest* 1987; **92**: 604.
- Pulmonary function in thalassemia major. FUNG KP, CHOW OKW *et al. Journal of Pediatrics* 1987; **111**: 534.
- Evaluation of bronchodilator responsiveness in mechanically ventilated patients. GAY PC, RODARTE JR *et al. American Review of Respiratory Disease* 1987; **136**: 880.
- Nocturnal hypoxemia in COPD. HUDGEL DW. *Chest* 1987; **92**: 579.
- Metabolic alkalosis and hypoventilation in humans. JAVAHERI S, KAZEMI H. *American Review of Respiratory Diseases* 1987; **136**: 1011.
- Facial cooling and perception of dyspnoea. LEADING ARTICLE. *Lancet* 1987; **2**: 836.
- Effects of lung inflation on nasal airway resistance in the anesthetized rat. LUNG MA. *Journal of Applied Physiology* 1987; **63**: 1339.
- Phrenic and external intercostal motoneuron activity during progressive asphyxia. MACEFIELD G, NAIL B. *Journal of Applied Physiology* 1987; **63**: 1413.
- Differences in respiratory patterns after acute and chronic pulmonary denervation. MARTIN-BODY RL, SINCLAIR JD. *Respiration Physiology* 1987; **70**: 205.
- The transfer factor (diffusing capacity) as a predictor of hypoxaemia during exercise in restrictive and chronic obstructive pulmonary disease. NORDENFELT I, STVENSSON G. *Clinical Physiology* 1987; **7**: 423.
- Cardiorespiratory patterns in viral septicemia. OKRENT DG, ABRAHAM E, WINSTON D. *American Journal of Medicine* 1987; **83**: 681.
- Plasma exudation and asthma. PERSSON CG. *Lung* 1988; **166**: 1.
- Specificity of pulmonary vascular lesions in primary pulmonary hypertension. A reappraisal. PIETRA GG, RUTTNER JR. *Respiration* 1987; **52**: 81.
- Respiration during sleep in kyphoscoliosis. SAWICKA EH, BRANTHWAITE MA. *Thorax* 1987; **42**: 801.
- Effect of a previous voluntary deep breath on laryngeal resistance in normal and asthmatic subjects. SEKIZAWA K, YANAI M *et al. Journal of Applied Physiology* 1987; **63**: 1406.
- Changes in breathing and the pharynx after weight loss in ob-

- structive sleep apnea. SURATT PM, MCTIER RF *et al. Chest* 1987; **92**: 631.
- Effects of ventilatory pattern on hyperinflation, airway pressures, & circulation in mechanical ventilation of patients with severe air-flow obstruction. TUXEN DV, LANE S. *American Review of Respiratory Disease* 1987; **136**: 872.
- Relation between upper airway volume and hyoid muscle length. VAN LUNTEREN E, HAXHIU MA, CHERNIACK N. *Journal of Applied Physiology* 1987; **63**: 1443.
- Flow-volume loop changes reflecting respiratory muscle weakness in chronic neuromuscular disorders. VINCKEN WG, ELLEKER MG, COSIO MG. *American Journal of Medicine* 1987; **83**: 673.
- Effect of high-frequency ventilation on lung mechanics at high transpulmonary pressure. WEINMANN GG, HUANG YC, MITZNER W. *Journal of Applied Physiology* 1987; **63**: 1544.
- Adrenergic control of airway function. ZAAGSMA J, GANAMSTERDAM RGM *et al. American Review of Respiratory Disease* 1987; **136** (Suppl): S45.

Treatment and medication

- The noninvasive respiratory care unit. BONE RC. *American Review of Respiratory Disease* 1987; **136**: 804.
- Nifedipine attenuates acute hypoxic pulmonary vasoconstriction in patients with chronic obstructive pulmonary disease. BURGHUBER OC. *Respiration* 1987; **52**: 86.
- Respiratory care in muscular dystrophy. HECKMATT JZ. *British Medical Journal* 1987; **295**: 1014.
- Effect of aminophylline on diaphragmatic contractility in patients with chronic obstructive lung disease. MURCIANO D, AUBIER M *et al. La Presse Medicale* 1987; **16**: 1628.
- Prognosis of noncardiac medical patients receiving mechanical ventilation in a veterans hospital. PAPADAKIS MA, BROWNER WS. *American Journal of Medicine* 1987; **83**: 687.

Central nervous system

Physiology

- Volume regulatory influx of electrolytes from plasma to brain during acute hyperosmolality. CSERR HF, DEPASQUALE M, PATLAK CS. *American Journal of Physiology* 1987; **253** (Part 2): 530.
- Sleep spindle activity changes in patients with affective disorders. DE MAERTELAER V, HOFFMAN G *et al. Sleep* 1987; **10**: 443.
- Effects of nutrients on brain function. DEFUDIS FV. In: ESSMAN WB, ed. *Nutrients and Brain Function*. Basel: S Karger, 1987; p. 11.
- Regulation of brain water and electrolyte contents: the possible involvement of central atrial natriuretic factor. DOCZI T, JOO F *et al. Neurosurgery* 1987; **21**: 454.
- Beta-receptor-mediated increase in cerebral blood flow during hypoglycemia. HOLLINGER BR, BRYAN RM. *American Journal of Physiology* 1987; **253** (Part 2): H949.
- Simultaneous determination of regional cerebral blood flow, glucose metabolism, and pH in acute experimental allergic encephalomyelitis. JUHLER M. *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 578.
- Clinical significance of sleep apnea in the elderly. KNIGHT H, MILLMAN RP *et al. American Review of Respiratory Disease* 1987; **136**: 845.
- Neurological consequences of magnesium deficiency: correlations with epilepsy. LEAVER DD, PARKINSON GB, SCHNEIDER KM. *Clinical and Experimental Pharmacology & Physiology* 1987; **14**: 361.
- Metabolic encephalopathies: opportunities and challenges. LOCKWOOD AH. *Journal of Cerebral Blood Flow and Metabolism* 1987; **7**: 523.
- Diagnosis and pathophysiology of the (obstructive) sleep apnea syndrome. RUSSI E. *Deutsche Medizinische Wochenschrift* 1987; **112**: 1543.

Treatment and medication

- Sciatica and epidural gas. BEATTY RA. *Neurosurgery* 1987; **21**: 537.

- Correlation of admission fibrin degradation products with outcome and respiratory failure in patients with severe head injury. CRONE KR, LEE KS, KELLY DL JR. *Neurosurgery* 1987; 21: 532.
- Cerebral blood flow and metabolism during isoflurane-induced hypotension in patients subjected to surgery for cerebral aneurysms. MADSEN JB, COLD GE *et al. British Journal Anaesthesia* 1987; 59: 1204.
- On-off phenomenon: relation of levodopa pharmacokinetics and pharmacodynamics. NUTT JG. *Annals of Neurology* 1987; 22: 535.

Endocrine and metabolic

Physiology

- Mechanisms of autoimmunity: relevance to the pathogenesis of type I (insulin-dependent) diabetes mellitus. BOSI E, TODD I *et al. Diabetes/Metabolism Reviews* 1987; 3: 893.
- Effects of lidocaine infusion on the sympathetic response to abdominal surgery. CASSUTO J, HOGSTROM S *et al. Anesthesia and Analgesia* 1987; 66: 1008.
- GABA receptor stimulation increases the release of vasopressin and oxytocin in vitro. FJALLAND B, CHRISTENSEN JD, GRELL S. *European Journal of Pharmacology* 1987; 142: 155.
- Modulation of cardiovascular reflexes by arginine vasopressin. FLORAS JS, AYLWARD PE *et al. Canadian Journal of Physiology and Pharmacology* 1987; 65: 1717.
- Hepatic circulation during surgical stress and anesthesia with halothane, isoflurane, or fentanyl. GELMAN S, DILLARD E, BRADLEY EL. *Anesthesia and Analgesia* 1987; 66: 936.
- Cytochromes-P-450 and the regulation of steroid synthesis. HALL PF. *Steroids* 1986; 48: 133.
- Skeletal muscle oxygen availability during respiratory acid-base disturbances in cats. HAMPSON NB, JOBSIS-VANDERVELT FF. *Respiration Physiology* 1987; 70: 143.
- Trauma induced increases in plasma vasopressin and angiotensin II. HILTON JG, MARULLO DS. *Life Sciences* 1987; 41: 2195.
- Vasoconstrictor role for vasopressin in conscious, sodium-depleted rats. JOVER B, DUPONT M *et al. American Journal of Physiology* 1987; 253 (Part 2): H763.
- Effects of intraventricular injections of galanin on neuroendocrine functions in male rat. Possible involvement of hypothalamic catecholamine neuronal systems. MELANDER T, FUXE K *et al. Acta Physiologica Scandinavica* 1987; 131: 25.
- Cocaine induced secretion of ACTH, beta-endorphin, and corticosterone. MOLDOW RL, FISCHMAN AJ. *Peptides* 1987; 8: 819.
- Arginine vasopressin and oxytocin in the bovine adrenal gland. NUSSEY SS, PRYOR-JONES RA *et al. Journal of Endocrinology* 1987; 115: 141.
- The renal afferent nerves in the pathogenesis of hypertension. OPARIL S, SRIPAIROJTHIKOON W *et al. Canadian Journal of Physiology and Pharmacology* 1987; 65: 1548.
- Intrinsic and synaptic regulation of vasopressinergic neurons. RENAUD LP In: MCCANN SM, WEINER RI eds., *Integrative neuroendocrinology: molecular, cellular and clinical aspects*. Basel: S Karger, 1987; p. 46.
- Atrial natriuretic peptide protects against acute ischemic renal failure in the rat. SHAW SG, WEIDMANN P *et al. Journal of Clinical Investigation* 1987; 80: 1232.
- Renal reflexes in the regulation of blood pressure and sodium excretion. STELLA A, GOLIN R *et al. Canadian Journal of Physiology and Pharmacology* 1987; 65: 1536.
- Impaired glucose handling in active rheumatoid arthritis: relationship to the secretion of insulin and counter-regulatory hormones. SVENSON KLG, LUNDQVIST G *et al. Metabolism Clinical and Experimental* 1987; 36: 940.
- Glucose transport into skeletal muscle-influence of contractile activity, insulin, catecholamines and diabetes mellitus. WALL-

BERG-HENRIKSSON H. *Acta Physiologica Scandinavica* 1987; 131 (Suppl): 1.

Endocrine and metabolic

Treatment and medication

- Clinical pharmacokinetics of some newer diuretics. BEERMAN B, GRIND M. *Clinical Pharmacokinetics* 1987; 13: 254.
- Peripheral nerve function in patients with painful diabetic neuropathy treated with continuous subcutaneous insulin infusion. BERTELSMANN FW, HELMANS JJ *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1987; 50: 1337.
- Inhibitory effect of frusemide on sympathetic vasoconstrictor responses; dependence on a renal hormone and the vascular endothelium. GERKENS JF. *Clinical and Experimental Pharmacology & Physiology* 1987; 14: 371.
- Probenecid interferes with the natriuretic action of furosemide. HSIEH YY, HSIEH BS *et al. Journal of Cardiovascular Pharmacology* 1987; 10: 530.
- 1-desamino-8-d-arginine vasopressin (desmopressin) decreases operative blood loss in patients having Harrington rod spinal fusion surgery. KOBRINSKY NL, LETTS RM *et al. Annals of Internal Medicine* 1987; 107: 446.
- Insulin resistance following nocturnal hypoglycaemia in insulin-dependent diabetes mellitus. KOLLIND M, ADAMSON U, LINS PE. *Acta Endocrinologica* 1987; 116: 314.
- Neurofunctional testing for the detection of diabetic peripheral neuropathy. SOSENKO JM, GADIA MT *et al. Archives of Internal Medicine* 1987; 147: 1741.

Pain

Physiology

- Involvement of endogenous opioid peptides in acupuncture analgesia. HE L. *Pain* 1987; 31: 99.
- Why do patients with severe arterial insufficiency get pain during sleep? JELNES R, BULOW J *et al. Scandinavian Journal of Clinical & Laboratory Investigation* 1987; 47: 649.
- CSF distribution of opioids in animals and man. PAYNE R. *Acta Anaesthesiologica Scandinavica* 1987; 31 (Suppl. 85): 38.

Treatment and medication

- Cocaine and morphine interaction in acute and chronic cancer pain. KAIKO RF, KANNER R *et al. Pain* 1987; 31: 35.
- Intraspinal narcotics: non-malignant pain. MURPHY TM, HINDS S, CHERRY D. *Acta Anaesthesiologica Scandinavica* 1987; 31 (Suppl. 85): 75.
- Intraspinal morphine for cancer pain. VENTAFRIDDA V, SPOLDI E, DE CONNO F. *Acta Anaesthesiologica Scandinavica* 1987; 31 (Suppl. 85): 47.

Other

Treatment and medication

- Absorption of an aqueous solution of a new synthetic somatostatin analogue administered to man by gavage. KOHLER E, DUBEROW-DREWE M *et al. European Journal of Clinical Pharmacology* 1987; 33: 167.
- Effect of timolol on intraocular pressure elevation following argon laser iridotomy. LIU PF, HUNG PT. *Journal of Ocular Pharmacology* 1987; 3: 249.
- Comparison of the airway response to eye drops of timolol and its isomer L-714,465 in asthmatic subjects. RICHARDS R, TATTERSFIELD AE. *British Journal of Clinical Pharmacology* 1987; 24: 485.

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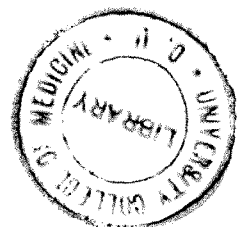
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Experiences with Propofol

**Papers based on proceedings of an international symposium at the Royal College of Physicians
in November 1987.**

Edited by

M. MORGAN AND J.N.LUNN



Foreword

Propofol, the subject of this symposium held in London in November 1987, was studied extensively in its original formulation between 1977 and 1981. Those of us who used the early preparation were impressed by the quality of anaesthesia obtained, and particularly by the speed and quality of recovery. That formulation was withdrawn to avoid the potential problems of immune responses to the vehicle, Cremophor EL.

The new formulation of propofol as an aqueous emulsion was introduced in July 1983. Early studies to satisfy the drug licensing requirements in the United Kingdom confirmed the previous enthusiasm for the advantageous properties of the drug but identified certain minor sequelae which might be considered disadvantageous.

The first symposium on propofol held in July 1985 confirmed the benefits of the new formulation of propofol for induction and maintenance of anaesthesia for short surgical procedures but also identified a number of other potential applications such as continuous intravenous infusion, both for anaesthesia and for sedation in intensive care units.

An Industry Forum held in September 1986 in conjunction with the VIIth European Congress of Anaesthesiology in Vienna, concentrated specifically on the applications of propofol for intravenous sedation or maintenance of anaesthesia by continuous infusion. The quality of clinical scientific investigation has been pre-eminent throughout these various symposia, and this bodes well for this supplement which concentrates on the clinical experience with propofol, predominantly in the European context. The range of clinical applications is widening rapidly as the drug finds its rightful place in the armamentarium of the clinician.

*Sir Humphry Davy Department of Anaesthesia,
University of Bristol*

C. PRYS-ROBERTS

Total intravenous anaesthesia with propofol and alfentanil by computer-assisted infusion

J. SCHÜTTLER, S. KLOOS, H. SCHWILDEN AND H. STOECKEL

Summary

The combination of propofol and alfentanil was administered to 20 patients for total intravenous anaesthesia during general surgery. The infusion rates for both drugs were controlled by microprocessors in order to institute constant blood levels adapted to the patients' varying needs. The mean blood level of propofol required for adequate hypnosis during anaesthesia was 2.42 µg/ml (SD 0.43). Awakening occurred 7.9 minutes (SD 3.4) after the end of the infusion, at a propofol blood level of 1.59 µg/ml (SD 0.34). The plasma level of alfentanil was 285 ng/ml (SD 72) during major noxious stimulation and 148 ng/ml (SD 56) during minor stimulation. The computer-assisted infusions showed a measured/predicted ratio of 1.01 (SD 0.28) for alfentanil and 0.88 (SD 0.22) for propofol. This indicates that the administration device used in this study is reasonably reliable. The technique of total intravenous anaesthesia was characterised by a smooth induction without significant haemodynamic alterations, by good control during anaesthesia and by a very fast recovery without major side effects.

Key words

Anaesthetics, intravenous; propofol.
Equipment; computer, infusion pumps.

The clinical acceptability of techniques for total intravenous anaesthesia is determined mainly by two factors. Firstly, the drugs for this purpose should guarantee, besides the lack of major side effects, a reasonable degree of control of their main pharmacodynamic effects, which will depend mainly upon their pharmacokinetic behaviour. Secondly, devices for the administration of intravenous anaesthetics have to be as easy to use as vaporizers for inhalational anaesthetics.

The pharmacokinetic properties of alfentanil^{1,2} make it well suited to suppress the response to noxious stimuli adaptively during surgical interventions. Total intravenous anaesthesia with alfentanil combined with etomidate⁵ proved to be feasible, but etomidate is not ideal for this purpose because of its adrenocortical depressant effects. Propofol in its emulsion formulation appears to be a good alternative, especially with regard to its rapid elimination.^{6,7} The combined administration of propofol and alfentanil by a microprocessor controlled-infusion device, as easy to use as a vaporiser, was therefore investigated for total intravenous anaesthesia.

Methods

Written informed consent after institutional approval was obtained from 20 patients of ASA grade 1 or 2, aged 18-52 years, weight 52-85 kg, who were scheduled for general surgery. They were premedicated with flunitrazepam 2 mg orally the evening before surgery and 1 mg orally one hour before anaesthesia. Anaesthesia was induced after the intravenous injection of vecuronium 2 mg, by a computer-controlled infusion of propofol which was aimed at a constant blood level of 2.5 µg/ml. The infusion of alfentanil was started 30 seconds later and aimed at a constant plasma level of 100 ng/ml; this was maintained for 5 minutes and reintroduced at the start of surgery. A large vein in the forearm was used to place the indwelling catheter used for infusion. Vecuronium 3 mg was given intravenously and tracheal intubation was performed 2 minutes later, after ventilation of the lungs with oxygen by face-mask. The lungs were then ventilated with oxygen in air (F_{IO_2} 0.5) to maintain a normal P_{aCO_2} . The blood level of propofol was increased in steps of 0.25 µg/ml if signs of lightening of

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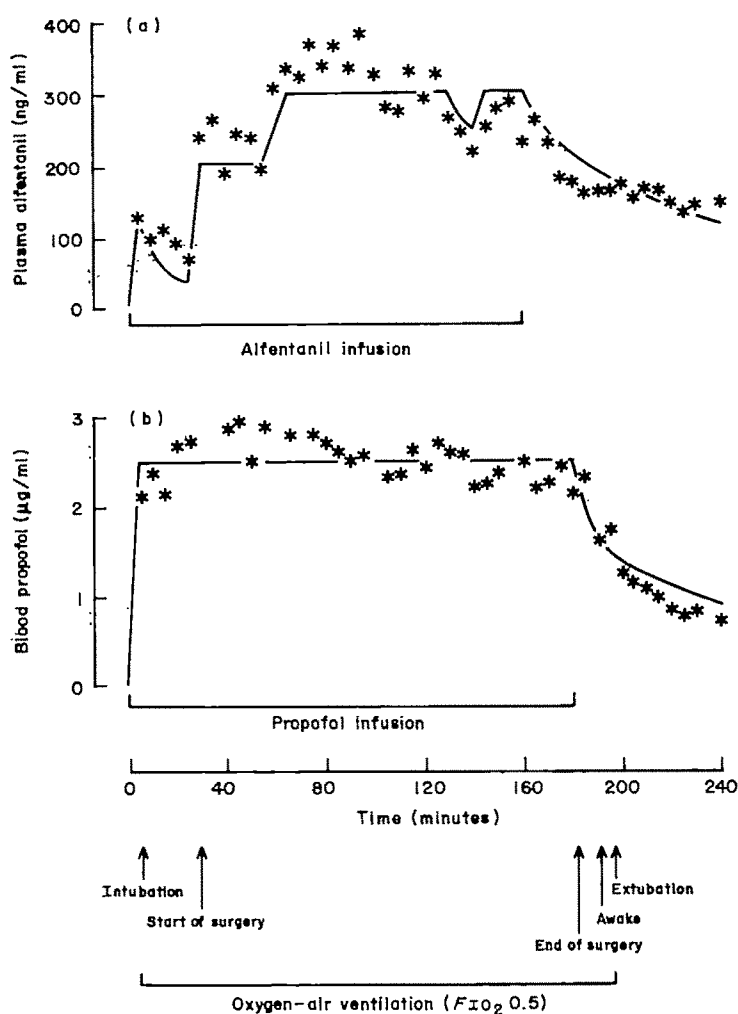


Fig. 1. (a) Plasma levels of alfentanil and (b) blood levels of propofol as predicted (—) by computer-assisted interactive infusions (solid line) and as actually measured (asterisks) in one representative patient who received the described anaesthetic technique.

anaesthesia occurred during the interval between induction and the start of surgery. The infusion of alfentanil was started again at the time of skin incision. Plasma alfentanil levels were adjusted according to the degree of noxious stimulation during the surgical procedures. In general, the administration of alfentanil was stopped 30 minutes before the end of operation. The infusion of propofol was kept stable until the last suture of skin closure. Recovery was assessed as the time from the end of the propofol infusion until the patient responded to verbal commands, and until extubation and proper orientation.

Blood levels of propofol were measured by high-performance liquid chromatography⁷ and plasma levels of alfentanil by radio-immunoassay.⁸ The measured concentrations were related to the predictions made by the computer-assisted administration device. Measured/predicted ratios (m/p ratios) were calculated and linear regression analysis was performed. Results are given as means (standard deviation). Statistical analysis was performed by Student's *t*-test.

The infusion schemes were based upon algorithms described previously.⁹ The device differed from that in previous studies⁵ because the anaesthetist had to operate only one dial to preset the blood level of choice, similar to a

vaporizer for inhalational anaesthetics. The pharmacokinetic data incorporated into the system were taken from previous studies on alfentanil¹ and propofol.¹⁰

Results

A representative example of plasma alfentanil and blood propofol levels during computer-assisted total intravenous anaesthesia is shown in Fig. 1. The blood level of propofol in this patient was kept constant at 2.5 µg/ml for the entire duration of anaesthesia. The plasma level of alfentanil was adapted in a stepwise manner at the start of surgery. The alfentanil infusion was terminated 20 minutes before the end of operation. There is good agreement between the predicted and measured concentrations of both drugs in this patient. Regression analysis for the predicted and measured values showed a highly significant correlation ($p < 0.001$) for both alfentanil (Fig. 2) and propofol (Fig. 3), although the variability of the propofol data was greater. There was a tendency to overpredict the propofol concentration which is indicated by an overall m/p ratio of 0.88 (SD 0.22) (Table 1). The m/p ratio for alfentanil, 1.01 (SD 0.28) (Table 1), in contrast, is nearly optimal.

The clinical results are summarised in Table 1. The mean duration of surgery was 104 minutes (SD 43). Propofol was

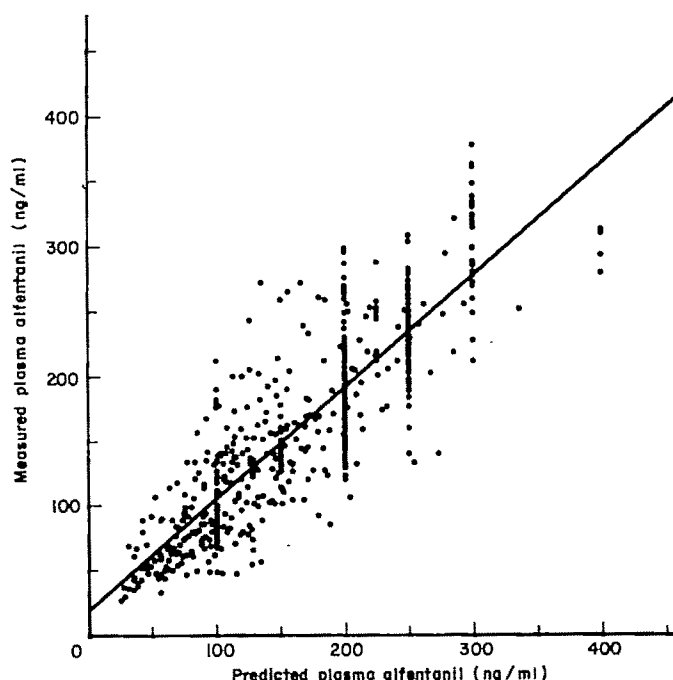


Fig. 2. Correlation between predicted plasma levels of alfentanil and measured concentrations during and after computer-assisted infusion. $n = 565$, $r = 0.87$, $m = 0.86$, $b = 19.3$.

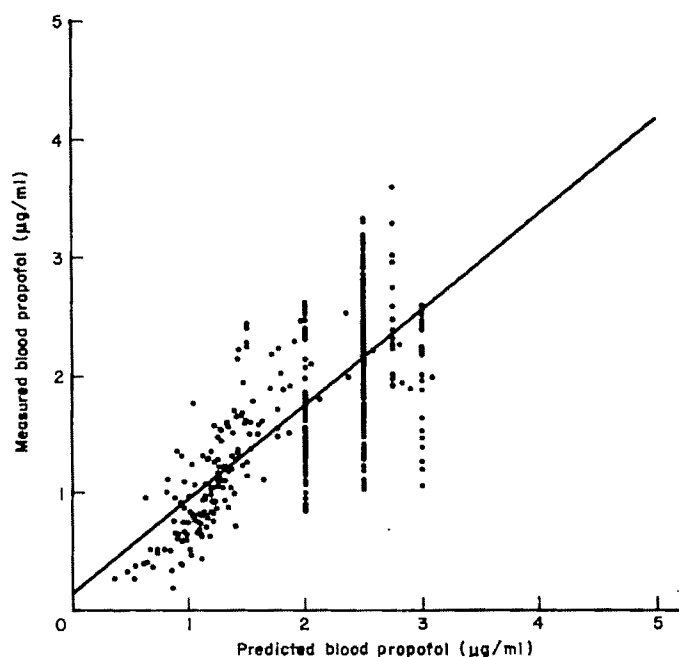


Fig. 3. Correlation between predicted blood levels of propofol and measured concentrations during and after computer assisted infusion. $n = 508$, $r = 0.75$, $m = 0.81$, $b = 0.13$.

infused for 131 minutes (SD 42) with a total dose of 838.7 mg (SD 193.8). The total dose for alfentanil was 13.8 mg (SD 5.3) with an infusion time of 112 minutes (SD 45). Induction of anaesthesia was smooth and without any side effects. Intubation could be performed in all subjects without difficulty. The haemodynamic response during this period (Fig. 4) did not exhibit significant alterations. It was possible to control the depth of anaesthesia satisfactorily during maintenance. Recovery was short; patients awoke 7.9 minutes (SD 3.4) after the end of the propofol infusion,

and extubation could be performed after 11.9 minutes (SD 3.8). All patients were fully orientated and clear-headed by this time. Postoperative nausea occurred in only one case and no other side effects were observed.

Discussion

The results of this investigation demonstrate that the practicability of total intravenous anaesthesia can be increased to

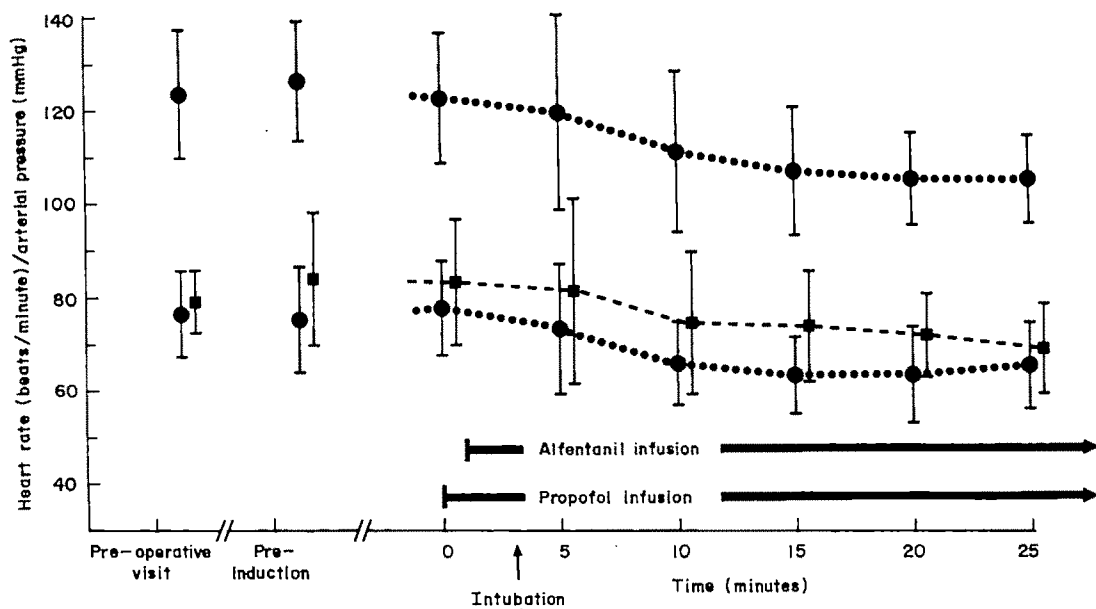


Fig. 4. Haemodynamic response during induction of anaesthesia in 20 patients with the described technique of total intravenous anaesthesia (mean, SD). ■, Heart rate; ●, arterial blood pressure (mmHg).

Table 1. Clinical data and drug concentrations in 20 patients undergoing total intravenous anaesthesia with propofol and alfentanil by computer-assisted infusion. Values expressed as mean (SD).

	Propofol	Alfentanil
Duration of surgery, minutes	104 (43)	
Duration of infusion, minutes	131 (41.8)	112 (44.5)
Total dose, mg	838.7 (193.8)	13.8 (5.3)
Maximum therapeutic concentration	2.42 µg/ml (0.43)	285 ng/ml (72)
Minimum therapeutic concentration	2.11 µg/ml (0.45)	148 ng/ml (56)
Time to awakening, minutes	7.9 (3.4)	
Drug concentrations	1.59 µg/ml (0.34)	142 ng/ml (45)
Time to extubation or spontaneous ventilation and orientation, minutes	11.9 (3.8)	
Drug concentrations	1.37 µg/ml (0.31)	136 ng/ml (41)
Measured/predicted ratio (n = 1073)	0.88 (0.22)	1.01 (0.28)

a considerable degree by the use of modern administration techniques based upon microprocessor support. However, for this approach it is necessary to know mean population data for the pharmacokinetic behaviour of the drugs to be employed. It is normal to use a set of data generated in a small ($n = 6-10$), standardised study group^{1,6,7} if drug administration is based upon pharmacokinetic principles. An alternative approach² investigates larger group sizes ($n = 40-50$) to determine factors that are likely to influence the pharmacokinetic profile of a drug in a defined population. This study confirms the previous conclusion^{4,5} that a pharmacokinetic data set for alfentanil generated from a small group is widely¹ applicable as a basis for calculated dosage schemes, without any weight corrections, in adult patients. The overall m/p ratio of 1.01 (Table 1) reflects a nearly optimal result. Variation (Fig. 2), however, is caused by many factors such as between-patients variability, changes in haemodynamics during anaesthesia, concurrent medication or disease. Technical factors also have to be

taken into consideration; these include performance errors of the delivery device, errors at sampling, or measurement errors when drug concentrations are assessed. The greatest deviation of the measured alfentanil concentration from that predicted did not exceed 50% at therapeutic concentrations of 200–300 ng/ml (Fig. 2). The greatest deviation of measured from predicted blood levels for propofol was somewhat higher in the therapeutic range (2.5–3.0 µg/ml) but did not exceed 60% (Fig. 3). The total overall prediction error for propofol, as reflected by the m/p ratio of 0.880, indicates slight overestimation for the mean pharmacokinetic data set which was generated in volunteers in an infusion study for pharmacodynamic modelling.¹⁰ This may be explained by a pharmacokinetic interaction between alfentanil and propofol or because an inappropriate set of pharmacokinetic data, not applicable for clinical anaesthesia, was used. This needs further investigation.

Whether the observed variability is tolerable or not can be answered as follows. The performance of the system is acceptable when the mean variation of measured concentrations around the predicted values is about 20–30% and when the maximal variation does not exceed 50–60%. Under these conditions the blood level selected by the anaesthetist will be achieved in every case. If patient variability causes deviations of this magnitude the ability of the device to respond allowed the blood level to be adjusted easily and as necessary. The pharmacokinetic data set provided to the delivery system should be modified, however, if the variability becomes greater and if the total bias exceeds 10–20%.

The drugs chosen for total intravenous anaesthesia in this study permitted good control of the desired effect. There are normally no difficulties if the pharmacodynamic effect is to be enhanced: this is achieved simply by dosage schemes that generate either linearly increasing blood levels or produce elevations in a stepwise manner.⁹ However, it is necessary to rely upon the pharmacokinetic decay profile of a drug after infusion if swift disappearance of pharmacological action at the end of anaesthesia is of interest. Here

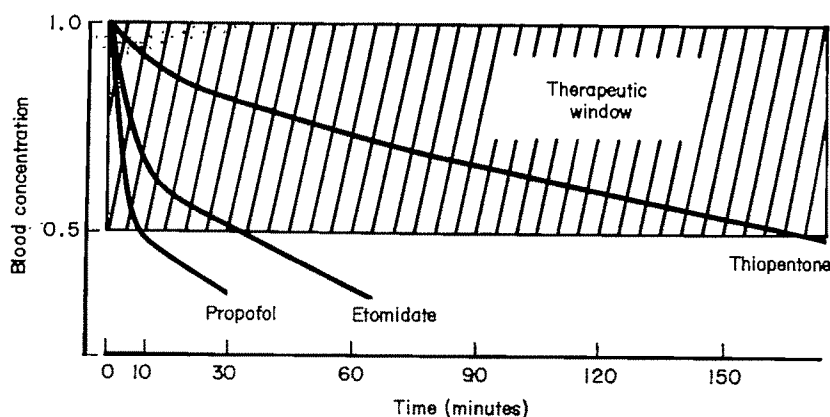


Fig. 5. Simulated blood level-decay from optimal to minimal therapeutic concentration after a 3-hour infusion of propofol, etomidate and thiopentone. Concentrations are given as fractions of the optimal therapeutic concentration for each drug at the end of infusion.

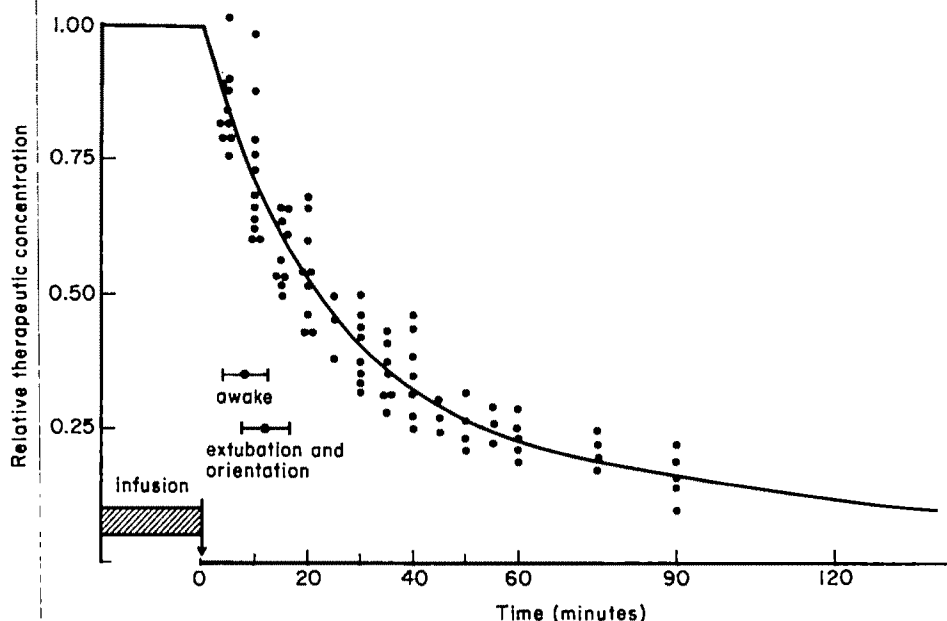


Fig. 6. Relative blood levels ($n = 89$) of propofol in 20 patients during recovery from total intravenous anaesthesia. Concentrations are given as fractions of the individual therapeutic concentrations at the end of infusion.

predictions based upon dynamic-pharmacokinetic modelling indicate propofol to be a favourable intravenous anaesthetic (Fig. 5) compared to etomidate and thiopentone.

The individual propofol blood level decay curves of the 20 patients after cessation of the infusion reflected the predictions closely (Fig. 6). The rapid disappearance of propofol from the blood even after prolonged infusion, is responsible for the excellent control of its pharmacodynamic effects and allows fast recovery (Table 1). The decay of alfentanil after infusion^{3,11} is not as fast, so long recovery periods are likely if high plasma levels (300–500 ng/ml) are maintained until the end of surgery. Therefore, it is necessary to adjust the alfentanil plasma concentration carefully and, whenever possible, to terminate the infusion about 30 minutes before the end of surgery. Recovery can be kept short (Table 1) if these rules are followed, with reasonable extubation times of the order of 10 minutes postoperatively.

Computer-assisted total intravenous anaesthesia with propofol and alfentanil proved to be very satisfactory from a clinical point of view. Haemodynamic variables did not

change significantly during induction (Fig. 4), and the pronounced hypotension^{12,13} observed after bolus injections of propofol 2.0 mg/kg did not occur in the present study. This can be explained by the difference in dosing technique. The initial bolus dose of about 65 mg is delivered in the first minute by the computerised infusion to achieve propofol blood levels of 2.5 $\mu\text{g/ml}$, the target concentration. Thereafter the infusion rate is about 10 mg/minute and declines exponentially to 5 mg/minute. Hypotension can be avoided in ASA grade 1 or 2 patients by this dosage scheme. Induction time appears to be prolonged in comparison to the higher bolus injections but this was not a disadvantage in this protocol which included vecuronium as the sole muscle relaxant. In addition, this dosage scheme compensates for the delayed onset of action of propofol,¹⁰ and contrasts with relatively large bolus injections often used to overcome this effect. Pain on injection, movement during induction, restlessness and vomiting during recovery were not seen; nausea occurred in one case and postoperative analgesia was required in two. There was euphoria in 14 out of 20 patients during recovery.

The combined administration of propofol and alfentanil by computer-assisted infusion proved to be a very satisfactory alternative to inhalational anaesthesia with the same degree of control and lack of major side effects.

Acknowledgments

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References

- SCHÜTTLER J, STOECKEL H, Alfentanil (R 39209), ein neues kurzwirkendes Opioid. Pharmacokinetik und erste klinische Erfahrungen. *Anaesthetist* 1982; **31**: 10–14.
- MAITRE PO, Vozeh S, Heykants J, Thomson DA, Stanski DR. Population pharmacokinetics of alfentanil. The average dose-plasma concentration relationship and interindividual variability in patients. *Anesthesiology* 1987; **66**: 3–12.
- SCHÜTTLER J, STOECKEL H, SCHWILDEN H, LAUVEN PM. Pharmakokinetisch begründete Infusionsmodelle für die Narkoseführung mit Alfentanil. In: DOENICKE A, ed. *Alfentanil*. Berlin: Springer, 1986; 42–51.
- AUSEMS ME, HUG CC Jr, STANSKI DR, BURM AGL. Plasma concentrations of alfentanil required to supplement nitrous oxide anesthesia for general surgery. *Anesthesiology* 1986; **65**: 362–73.
- SCHÜTTLER J, SCHWILDEN H, STOECKEL H. Pharmacokinetics as applied to total intravenous anaesthesia. Practical implications. *Anaesthesia* 1983; **38** (Suppl.): 53–6.
- SCHÜTTLER J, STOECKEL H, SCHWILDEN H. Pharmacokinetic and pharmacodynamic modelling of propofol ('Diprivan') in volunteers and surgical patients. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 53–4.
- COCKSHOT ID, BRIGGS LP, DOUGLAS EJ. Pharmacokinetics of propofol in female patients. Studies using single bolus injections. *British Journal of Anaesthesia* 1987; **59**: 1103–10.
- SCHÜTTLER J, WHITE PF. Optimization of the radioimmunoassays for measuring fentanyl and alfentanil in human serum. *Anesthesiology* 1984; **61**: 315–20.
- SCHWILDEN H. A general method for calculating the dosage scheme in linear pharmacokinetics. *European Journal of Clinical Pharmacology* 1982; **20**: 379–86.
- SCHÜTTLER J, SCHWILDEN H, STOECKEL H. Pharmacokinetic-dynamic modeling of Diprivan. *Anesthesiology* 1986; **65**: A549.
- HULL CJ. The pharmacokinetics of alfentanil in man. *British Journal of Anaesthesia* 1983; **55** (Suppl. 2): 157S–64S.
- COATES DP, PRYS-ROBERTS C, SPELINA KR, MONK CR, NORLEY I. Propofol ('Diprivan') by intravenous infusion with nitrous oxide: dose requirements and haemodynamic effects. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 76–9.
- STEPHAN H, SONNTAG H, SCHENK HD, KETTLER D, KHAMBATA HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; **58**: 969–75.

Disposition kinetics of propofol during alfentanil anaesthesia

E. GEPTS, K. JONCKHEER, V. MAES, W. SONCK AND F. CAMU

Summary

The pharmacokinetics of a constant rate infusion of propofol were studied in 11 patients who received total intravenous anaesthesia for ENT surgery. Alfentanil was administered as an exponentially decreasing infusion using a computer-assisted infusion device with a constant target plasma alfentanil concentration of 300 ng/ml. Propofol was infused at a constant rate of 6 mg/kg/hours. Plasma alfentanil concentrations were determined by gas chromatography and whole blood propofol concentrations by high-performance liquid chromatography in arterial blood samples collected at selected times during and up to 8 hours after infusion. Pharmacokinetic modelling of the blood propofol concentration–time data indicated that a three-compartment open model with central elimination was most appropriate. Derived pharmacokinetic parameters were in agreement with previous studies on the pharmacokinetics of propofol. The plasma alfentanil concentrations in 10 patients significantly exceeded the expected values at any time during the infusion. The population mean bias amounted to 20.2% (SD 12.6). Only three data sets were significantly underestimated after the infusion was stopped (mean bias 11.9% (SD 25.5)). The elimination half-life of alfentanil was approximately 75 minutes (SD 21). We conclude that alfentanil does not interfere with the pharmacokinetic profile of propofol but that propofol induces higher plasma alfentanil concentrations than expected.

Key words

Anaesthetics, intravenous: propofol.

Analgesics, narcotic; alfentanil.

Pharmacokinetics.

Propofol is a short-acting hypnotic agent that is effective for maintenance of anaesthesia when given intravenously as repeated bolus injections or as a continuous infusion. Few cumulative effects have been reported. The disposition kinetics of propofol were studied after bolus injection¹ and during and after different infusion rates,² and appeared to be linear within the therapeutic range used. The drug is rapidly cleared from blood but it is also extensively distributed, which results in a long terminal half-life in the range of 350 minutes. Clinical experience indicates that lower infusion rates of propofol are needed in the presence of potent analgesic drugs. Competition for distribution, tissue binding and metabolic inactivation may contribute to the final pharmacological interaction that is observed.

We studied the disposition kinetics of an infusion of propofol during analgesic anaesthesia and compared it to previously reported infusion kinetics of propofol given as the sole anaesthetic agent. Alfentanil was chosen as the analgesic drug: it is a short-acting fentanyl derivative that is pharmacokinetically suitable for the provision of stable surgical analgesia when administered as a continuous infusion.^{3,4} We postulated that a pharmacokinetic interaction between propofol and alfentanil could be respon-

sible for the decreased amount of propofol needed for maintenance of anaesthesia.

Methods

Eleven Caucasian patients, two women, scheduled for septoplasty were selected and gave informed consent. All were of ASA grade 1 or 2. Age, weight and height averages and ranges were 35 (24–51) years, 73.5 (58.5–102) kg and 173 (164–182) cm, respectively. Glycopyrronium 0.4 mg was administered intramuscularly 30–60 minutes before induction of anaesthesia. An indwelling intravenous cannula was placed in a forearm vein for infusion of the anaesthetic agents and for fluid replacement. Arterial blood pressure, heart rate and ECG were monitored.

An exponentially decreasing infusion of alfentanil was started using a computer-assisted infusion device (TIAC, Janssen Pharmaceutica Instruments) in order to reach and maintain a target alfentanil plasma concentration of 300 ng/ml. The computer program used pharmacokinetic data for alfentanil from Schüttler and Stoeckel.⁵ The patient, still awake at this time, was asked repeatedly to breathe normally and was given oxygen by facemask. A cannula

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for blood sampling was inserted into the radial artery of the non-dominant hand after adequate collateral circulation was ascertained. Anaesthesia was then completed by an infusion of propofol at a constant rate of 6 mg/kg/hour. 1 mg/kg was given to facilitate tracheal intubation on loss of consciousness. Ventilation with oxygen-enriched air (F_{IO_2} 0.3) was mechanically controlled to maintain normocapnia. Atracurium 25–50 mg was administered when convenient, after the effect of the suxamethonium had worn off. No other anaesthetic drugs were used. Surgical conditions were always satisfactory and anaesthesia was stable except in one patient who developed moderate hypertension after 90 minutes of anaesthesia and received droperidol. Both infusions were terminated at the end of surgery and the spontaneous recovery of consciousness and respiratory function observed. Amnesia for the operative period was investigated during a postoperative interview.

Arterial blood samples (5 ml) were taken before drug administration and at 2, 4, 6, 8, 10, 20, 30, 40, 50, 60, 75, 90, 105 and 120 minutes after the start of the propofol infusion. Additional samples were taken as appropriate when the infusion continued beyond 120 minutes. Further samples were collected 2, 4, 6, 8, 10, 20, 40, 60, 90, 120, 180, 240, 300, 360, 420 and 480 minutes after the end of the infusion. Additional samples for propofol analysis were taken at the onset of unconsciousness and on return of consciousness if these endpoints did not coincide with any of the routine sampling times. The blood samples were collected in tubes that contained potassium oxalate and, after thorough mixing they were cooled to 4°C and stored at this temperature until analysis for blood propofol content using high-performance liquid chromatography as previously described in detail.²

Heparinised blood samples (10 ml) were taken prior to alfentanil and at approximately 5, 10, 20, 30, 40, 50, 60, 80, 100 and 120 minutes after the alfentanil infusion was started. Additional samples were collected at the start of spontaneous respiration and during further recovery at 30–

60-minute intervals as long as total blood loss did not exceed 300 ml. The samples were centrifuged and the plasma frozen at –20°C until analysis for alfentanil content. The plasma alfentanil concentrations were determined using gas chromatography.⁶

A bi- and tri-exponential structural model⁷ was fitted to the individual propofol blood concentration data sets using the extended least-squares curve fitting program ELSFIT.⁸ The goodness of fit of both functions to the data was compared using the Schwarz criterion⁹ and by visual assessment of the residuals of the individual propofol concentration values from the line of best fit. Derived pharmacokinetic parameters included drug concentration at steady state (C_{ss}), apparent volume of distribution (V_{dp}), volume of distribution at steady state (V_{ss}), volume of the central compartment (V_c), half-lives of distribution and elimination and total blood clearance (Cl_b). Microconstants for drug transfer between compartments and for elimination, were calculated from the compartmental model using standard equations.^{10,11} The Mann–Whitney *U*-test was used to investigate differences between these results and previously reported kinetics of propofol infusions, and to compare the propofol blood concentrations at the onset of unconsciousness and on the return of consciousness.

The measured alfentanil plasma concentrations were compared to the predicted concentrations. The prediction error, the mean prediction error (bias) and the precision (SD of bias) were calculated for each patient according to the method used by Ausems *et al.*¹² to evaluate the accuracy of the TIAC device. The degree of bias was considered to be statistically significant ($p < 0.05$) when the 95% confidence limits of the bias did not include zero. All data are expressed as mean values (SD).

Results

The duration of propofol infusion averaged 144 minutes (range 120–223). The propofol blood concentrations in-

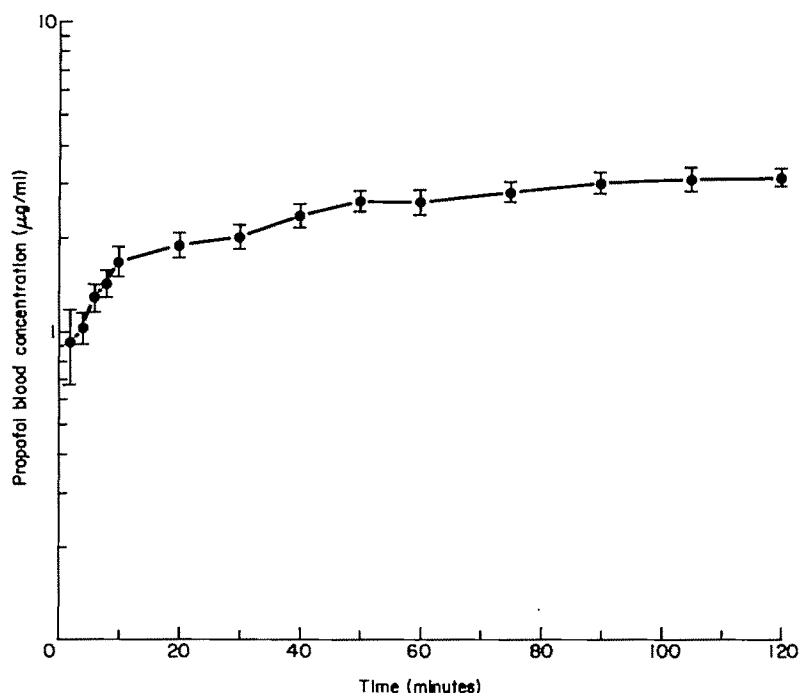


Fig. 1. Mean (SEM) propofol blood concentration as a function of time during propofol infusion at 6 mg/kg/hour.

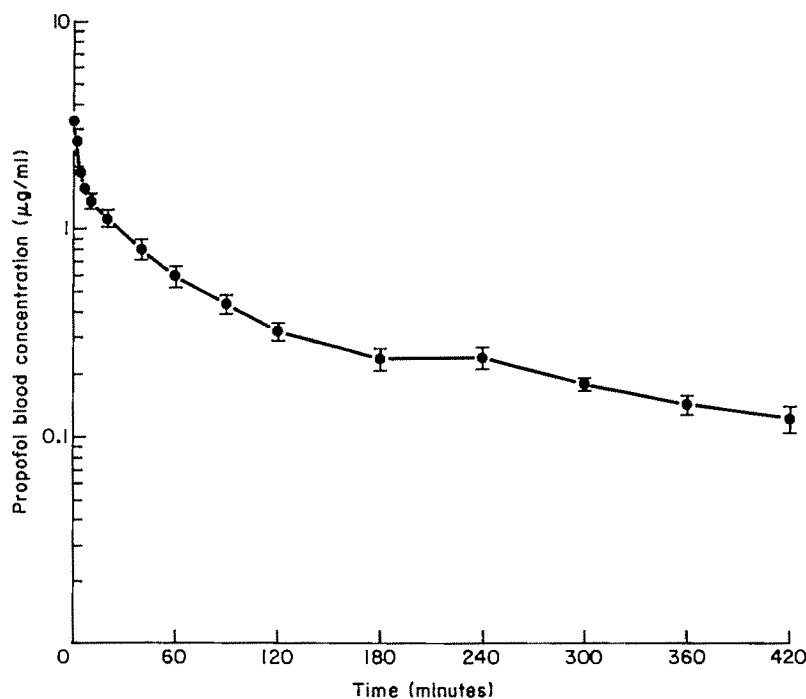


Fig. 2. Mean (SEM) propofol blood concentration as a function of time after the end of propofol infusion. For clarity the SEMs of the first 8 minutes of data are omitted.

itally increased rapidly with time, then more slowly and reached 81% (SD 13) of the steady state concentration C_{ss} after 120 minutes of infusion (Fig. 1). The onset of unconsciousness occurred after 8.6 minutes (SD 6.3) and at a propofol blood concentration that averaged 2.13 µg/ml (SD 0.84). The propofol blood concentrations after the end of the infusion decayed in a curvilinear manner with time (Fig. 2). Return of consciousness was observed after 14.1 minutes (SD 8.4) and at a propofol blood concentration that was significantly lower than the concentration measured at the onset of unconsciousness ($p < 0.55$) and averaged 1.29 µg/ml (SD 0.44).

The individual propofol blood concentration–time data were fitted best by a tri-exponential function in all patients. Derived pharmacokinetic parameters were calculated individually with the assumption of a three-compartmental open model with central elimination. Table 1 summarises the mean values of the present results as well as those from an earlier kinetic study performed during propofol in-

fusions administered to patients who underwent surgery under regional anaesthesia.² Statistical analysis did not demonstrate any significant difference between the pharmacokinetic parameters of the present 11 patients and the previous six patients who received propofol as an infusion at the same rate (6 mg/kg/hour) but as the sole intravenous anaesthetic agent. The mean values from the previous 18 study subjects, who received propofol infusions at 3, 6 or 9 mg/kg/hour during regional anaesthesia, were also fairly similar and no statistically significant differences could be demonstrated when compared with the present 11 subjects who received alfentanil for surgical analgesia.

The alfentanil plasma concentrations measured during the alfentanil infusion were generally above the predicted value of 300 ng/ml (Fig. 3). The prediction error decreased with time (Fig. 4) in six patients. Table 2 presents the individual values of the bias (mean prediction error), its precision (SD of the bias) and its statistical significance ($p < 0.05$) during and after infusion. All patients except

Table 1. Propofol pharmacokinetic parameters. Values expressed as mean (SD).

	Propofol 6 mg/hg/hour (n = 11) General anaesthesia (alfentanil)	Propofol 6 mg/hg/hour (n = 6)* Regional anaesthesia	Propofol 3, 6 or 9 mg/hg/hour (n = 18)* Regional anaesthesia
$t_{1/2\alpha}$, minutes	2.7 (1.3)	3.2 (1.1)	2.8 (2.1)
$t_{1/2\beta}$, minutes	23.6 (6.9)	37.5 (14.3)	31.4 (14.7)
$t_{1/2\gamma}$, minutes	280.9 (184.7)	385.5 (282.2)	355.0 (226.6)
C_{ss} , µg/minute	3.992 (0.825)	3.573 (0.748)	—
V_c , litres	19.697 (11.206)	16.408 (4.350)	16.924 (6.957)
V_d , litres	280.07 (220.33)	331.50 (256.93)	287.1 (212.85)
$V_{d\beta}$, litres	717.16 (391.97)	973.33 (498.49)	859.78 (432.31)
Cl_b , litres/minute	1.909 (0.482)	1.864 (0.269)	1.770 (0.322)
K_{10} , minutes ⁻¹	0.1180 (0.0548)	0.1212 (0.0359)	0.1190 (0.0351)
K_{12} , minutes ⁻¹	0.1105 (0.0629)	0.0696 (0.0465)	0.1140 (0.1051)
K_{13} , minutes ⁻¹	0.0514 (0.0411)	0.0455 (0.0196)	0.0419 (0.0155)
K_{21} , minutes ⁻¹	0.0570 (0.0181)	0.0330 (0.0216)	0.0550 (0.0558)
K_{31} , minutes ⁻¹	0.0047 (0.0024)	0.0032 (0.0012)	0.0033 (0.0013)

* Results from Gepts et al.²

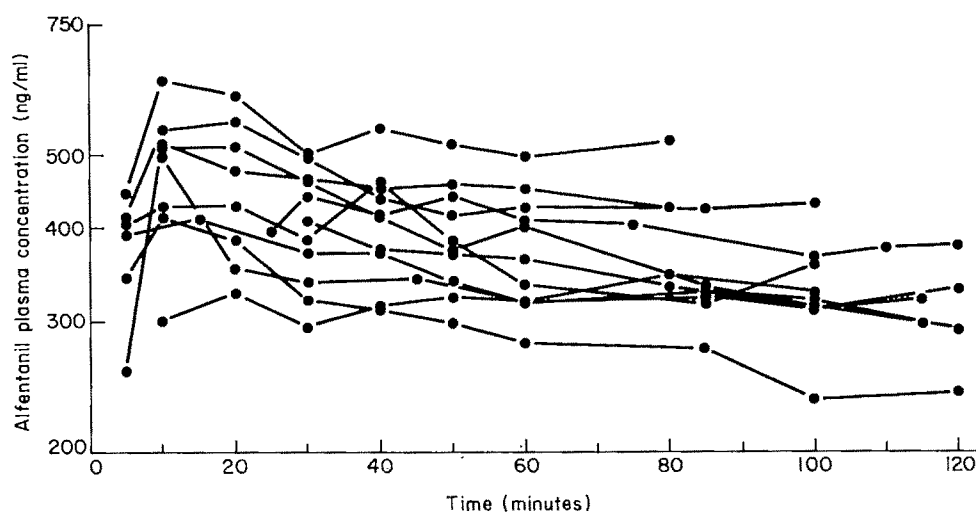


Fig. 3. Individual measured alfentanil plasma concentration as a function of time during alfentanil infusion.

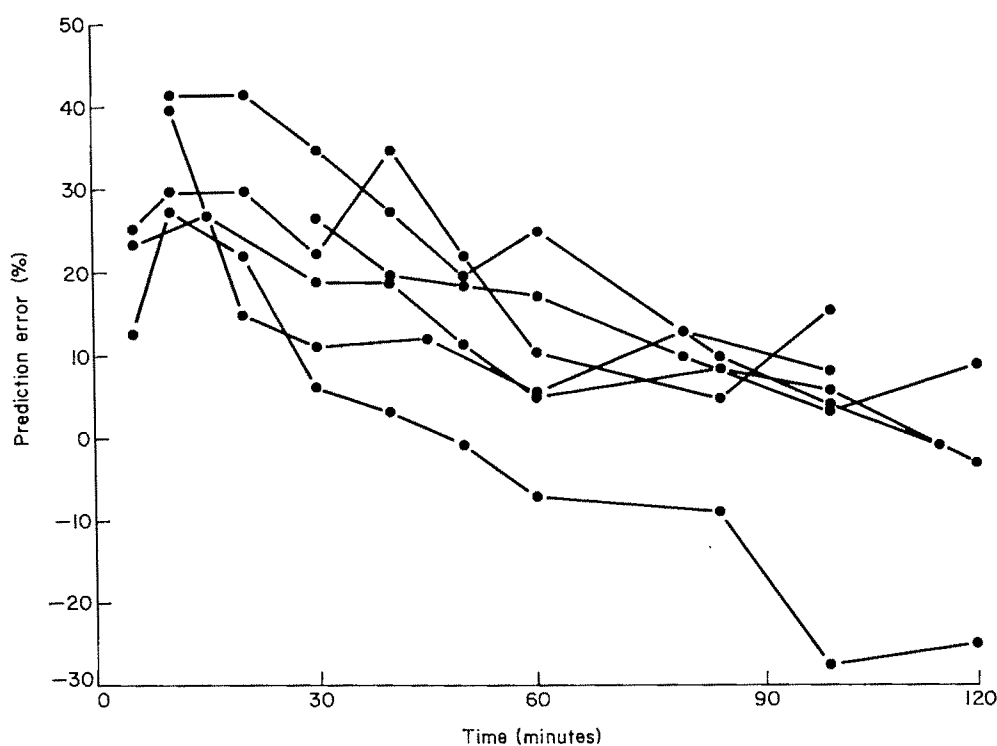


Fig. 4. Individual prediction error of alfentanil plasma concentration in percent as a function of time for six patients who showed decreasing prediction error with time.

one, demonstrated a significant positive bias during the alfentanil infusion. The population mean bias amounted to 20.2% (SD 12.6). The post-infusion data showed over- and underestimations (Fig. 5). The measured alfentanil plasma level exceeded the prediction systematically in four patients but only three data sets were statistically significant. The population mean bias after the infusion was stopped amounted to 11.9% (SD 22.5). Two patients were not included in the population mean value because only one plasma sample was available post infusion. The alfentanil plasma decay curves appeared to be linear on semilogarithmic plotting. An approximation of the elimination half-life could be derived using the standard feathering technique

on the post-infusion data in eight patients and it averaged 75 minutes. (SD 21).

Discussion

Drug interactions in general pharmacology are an exception rather than the rule but pharmacological interactions are frequently used in anaesthesia to potentiate desirable effects, to minimise side effects or to antagonise anaesthesia at the end of surgery. The drug interaction may be pharmacokinetic, pharmacodynamic or both. Better understanding of the mechanisms of drug interaction would improve the prediction of the ultimate pharmacological effect, its intensity and duration.

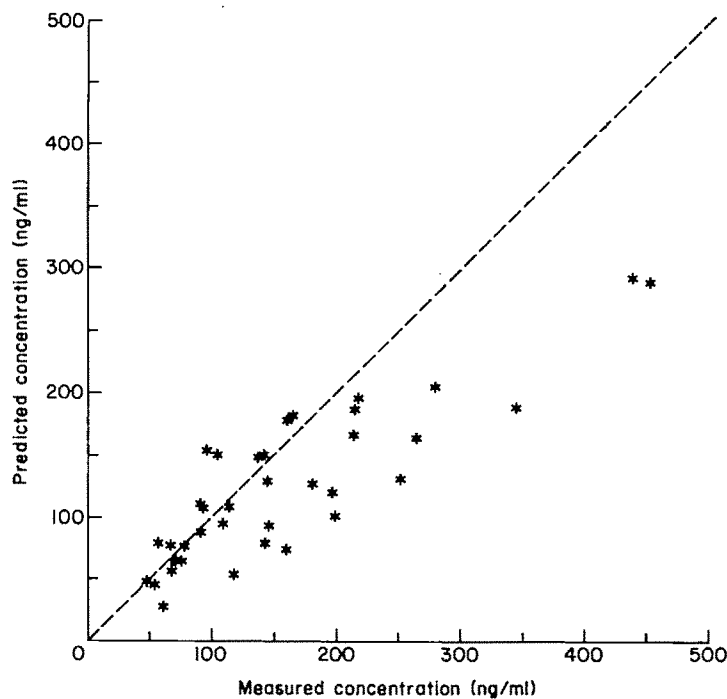


Fig. 5. Predicted alfentanil plasma concentration as a function of measured alfentanil plasma concentration after the end of alfentanil infusion. The interrupted line is the line of identity (predicted concentration = measured concentration).

Table 2. Mean prediction error (bias), precision (SD) and statistical significance of the individual alfentanil plasma concentrations measured.

Patient	During infusion		After infusion	
	n	Bias, % (SD)	n	Bias, % (SD)
1	8	28.6 (18.5)*	3	34.2 (2.3)*
2	9	25.1 (5.1)*	2	38.7 (3.2)*
3	7	15.0 (11.3)*	1	7.7
4	9	12.9 (9.8)*	3	23.6 (11.5)
5	8	43.1 (6.2)*	5	7.6 (18.1)
6	6	14.9 (7.9)*	1	-65.1
7	9	4.4 (3.3)*	3	-2.4 (12)
8	9	22.6 (15.7)*	5	1.2 (7.4)
9	9	21.7 (9.8)*	4	-23.5 (16.5)
10	9	34.0 (7.4)*	6	47.5 (2.7)*
11	10	0.2 (18.0) NS	4	-19.9 (22.8)
Population mean	93	20.2 (12.6)*	35	11.9 (25.5)

* Statistically significant at p < 0.05.

Propofol and alfentanil are both suitable for total intravenous anaesthesia when given by infusion, because their pharmacokinetic profiles predict little cumulative effects within therapeutic dosage ranges.¹⁻⁵ Clinical experience suggests that when propofol and alfentanil are used together to provide anaesthesia, the specific activity of each drug (hypnosis and analgesia, respectively) is potentiated. We postulated that a pharmacokinetic interaction could be at least partly responsible.

The present results indicate clearly that the disposition kinetics of propofol are unaffected in the presence of therapeutic plasma concentrations of alfentanil. Alfentanil, on the other hand, seems to exhibit pharmacokinetic alterations. The accuracy of the TIAC device when provided with the same mean pharmacokinetic parameters as in this study, has been investigated previously.^{12,13} Schuttler *et al.*¹³ used an alfentanil infusion with an infusion of etom-

idate. The duration of the alfentanil infusion was comparable to ours (106 minutes, SD 42) and the results indicated good correlation with prediction. Ausems *et al.*¹² studied the accuracy of TIAC for alfentanil dosing during surgical anaesthesia with nitrous oxide 66% in oxygen. There was a slight tendency to overpredict the alfentanil plasma level by 5-18% if the individual prediction errors were pooled, although this pooled bias did not reach statistical significance. Our results are at variance with these previous reports: systemic and significant underprediction of the alfentanil plasma concentration was observed and amounted to 20.2% (SD 12.6).

An increase in drug concentration in blood or plasma for a given dosage regimen, might be explained by two mechanisms: a decrease of the volume of distribution and/or a decreased elimination. The first would yield a shorter, the latter a longer half-life. The elimination half-life of alfentanil in the present study was approximated using plasma concentrations 3-4 hours after infusion and averaged 75 minutes (SD 21). This value is low compared to previous reports on the disposition kinetics of alfentanil during surgery^{5,14-16} but it is within the published range. Thus both mechanisms are probably implicated.

A decrease of the volume of distribution of alfentanil might result from increased plasma protein binding, which is improbable, or from decreased tissue binding. Alfentanil has a rather small volume of distribution (25-27 litres), which indicates low tissue affinity. Propofol, on the other hand, binds avidly to tissue components and exhibits a volume of distribution at steady state of about 300 litres.¹² Displacement of alfentanil from tissue binding sites by propofol, which possesses a greater tissue affinity, might reasonably be postulated, although similar examples of drug interaction are extremely rare.¹⁷ The liver extraction ratio of alfentanil ranges between 0.3 and 0.5. The clearance for alfentanil might thus be influenced by liver cell damage

and probably also by changes in liver blood flow.¹⁸ No evidence exists that propofol causes liver damage and decreased hepatic enzyme function but the haemodynamic effects during propofol and alfentanil anaesthesia may include a decreased hepatic blood flow.

Richter *et al.*¹⁹ studied the disposition kinetics of alfentanil after multiple bolus injections during an etomidate infusion. The derived pharmacokinetic parameters, terminal half-life and apparent volume of distribution, amounted to 65 minutes (SD 38) and 7.5 litres (SD 5), respectively. The half-life is not significantly shorter compared to previous studies but the volume of distribution appears to be very small. An alteration of the disposition kinetics of alfentanil during etomidate infusion, similar to the drug interaction observed in our study, has to be considered. However, the results of Schuttler *et al.*¹³ do not support this suggestion.

It is certainly useful to be aware of this drug interaction in clinical practice. Lower dosage regimens of alfentanil are recommended when propofol is used. Unusually important respiratory depression was observed in our department to follow low doses of alfentanil (0.25–0.5 mg intravenously) during propofol anaesthesia in patients who breathed spontaneously. We did not see similar problems when fentanyl was used as the analgesic. Fragen *et al.*²⁰ similarly reported that spontaneous respiration returned significantly sooner after fentanyl than after alfentanil in patients who received propofol anaesthesia.

We conclude that the pharmacological interaction observed when alfentanil and propofol are used together to provide anaesthesia, is due in part to an alteration of the disposition kinetics of alfentanil that results in alfentanil plasma levels higher than expected. However, supplementary homeostatic mechanisms in the evident mutual potentiation of both drugs cannot be excluded.

Acknowledgments

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References

1. KAY NH, SEAR JW, UPPINGTON J, COCKSHOTT I, DOUGLAS EJ. Disposition of propofol in patients undergoing surgery. A comparison in men and woman. *British Journal of Anaesthesia* 1986; **58**: 1075–79.
2. GEPTS E, CAMU F, COCKSHOTT ID, DOUGLAS EJ. Disposition of propofol administered as constant rate infusions in humans. *Anesthesia and Analgesia* (in press).
3. STANSKI DR, HUG CC Jr. Alfentanil—a kinetically predictable narcotic analgesic. *Anesthesiology* 1982; **57**: 435–8.
4. AUSEMS ME, HUG CC Jr, DE LANGE S. Variable rate infusion of alfentanil as a supplement to nitrous oxide anaesthesia for general surgery. *Anesthesia and Analgesia* 1983; **62**: 982–6.
5. SCHÜTTLER J, STOECKEL H. Alfentanil (R39209), ein neues kurzwirkendes opioid. *Pharmakokinetik und erste klinische Erfahrungen*. *Anaesthesist* 1982; **31**: 10–14.
6. WOESTENBORGHES R, MICHELSSEN L, HEYKANTS J. Rapid and sensitive gas chromatographic method for the determination of alfentanil and sufentanil in biological samples. *Journal of Chromatography* 1981; **224**: 122–7.
7. COLBURN WA. Simultaneous pharmacokinetic and pharmacodynamic modeling. *Journal of Pharmacokinetics and Biopharmaceutics* 1981; **9**: 367–88.
8. PECK CA, BEAL SL, SHEINER LB, NICHOLS AI. Extended least squares nonlinear regression: a possible solution to the 'choice of weights' problem in analysis of individual pharmacokinetic data. *Journal of Pharmacokinetics and Biopharmaceutics* 1984; **12**: 545–58.
9. SCHWARZ G. Estimating the dimension of a model. *Annals of Statistics* 1978; **3**: 461–4.
10. GIBALDI M, PERRIER D. *Pharmacokinetics*. New York: Marcel Dekker, 1982: 84–111.
11. LOO JCK, RIEGELMAN S. Assessment of pharmacokinetic constants from post infusion blood curves obtained after I.V. infusion. *Journal of Pharmaceutical Sciences* 1970; **59**: 53–55.
12. AUSEMS ME, STANSKI DR, HUG CC Jr. An evaluation of the accuracy of pharmacokinetic data for the computer assisted infusion of alfentanil. *British Journal of Anaesthesia* 1985; **57**: 1217–25.
13. SCHÜTTLER J, SCHWILDEN H, STOECKEL H. Pharmacokinetics as applied to total intravenous anaesthesia. Practical implications. *Anaesthesia* 1983; **38** (Suppl.): 53–6.
14. BOVILL JG, SEBEL PS, BLACKBURN C, HEYKANTS J. The pharmacokinetics of alfentanil (R 39209): a new opioid analgesic. *Anesthesiology* 1982; **57**: 439–43.
15. CAMU F, GEPTS E, RUCQUOI M, HEYKANTS J. Pharmacokinetics of alfentanil in man. *Anaesthesia and Analgesia* 1982; **61**: 657–61.
16. FRAGEN RJ, BOOU LHDJ, BAAK GJJJ, VREE TD, HEYKANTS J, CRUL JF. Pharmacokinetics of the infusion of alfentanil in man. *British Journal of Anaesthesia* 1983; **55**: 1077–81.
17. POND SM. Pharmacokinetic drug interactions. In: BENET LZ, MASSOUD N, GAMBARTOGLIO JG, eds. *Pharmacokinetic basis for drug treatment*. New York: Raven Press, 1984: 195–220.
18. CLAEYS MA, GEPTS E, CAMU F. Haemodynamic changes during bolus-infusion propofol anaesthesia. *British Journal of Anaesthesia* (in press).
19. RICHTER O, KLATTE A, ABEL J, FREYE E, HAAG W, HARTUNG E. Pharmacokinetic data analysis of alfentanil after multiple injections and etomidate-infusion in patients undergoing orthopedic surgery. *International Journal of Clinical Pharmacology, Therapy and Toxicology* 1985; **32**: 11–15.
20. FRAGEN RJ, HANSEN EHKH, DENISSEN PAF, BOOU LHDJ, CRUL JF. Disopropofol (ICI 35868) for total intravenous anaesthesia. *Acta Anaesthesiologica Scandinavica* 1983; **27**: 113–6.

Induction and maintenance of propofol anaesthesia

A manual infusion scheme

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C. PRYS-ROBERTS

Summary

A simple, manually controlled infusion scheme for continuous administration of propofol was derived by simulation of a computer algorithm designed to achieve a predetermined blood concentration of propofol within 2 minutes and to maintain a constant blood level for the duration of surgery. The manual infusion scheme for a target blood propofol concentration of 3 µg/ml, consisted of a loading dose of 1 mg/kg followed immediately by an infusion of 10 mg/kg/hour for 10 minutes, 8 mg/kg/hour for the next 10 minutes and 6 mg/kg/hour thereafter. An overall mean blood propofol concentration of 3.67 µg/ml was achieved within 2 minutes and maintained stable for the subsequent 80–90 minutes of surgery. The decrease of systolic and diastolic arterial pressures at induction was much less than that previously described after larger induction doses of propofol and there was a negligible haemodynamic response to laryngoscopy and intubation or to the subsequent surgery. The quality of induction and maintenance of anaesthesia was satisfactory in every patient.

Key words

Anaesthetics, intravenous; propofol
Anaesthetic techniques; infusion.

Propofol, by virtue of its favourable pharmacokinetic profile, has already achieved considerable popularity for induction and maintenance of anaesthesia for short duration surgery. The same profile has ensured its suitability for continuous infusion for prolonged surgery and also for sedation in intensive care units. The infusion rates of propofol to supplement nitrous oxide anaesthesia required to suppress movement in response to the initial surgical stimulus have been determined in patients who have received a variety of premedications.^{1–3} The whole blood concentrations required to achieve such anaesthetic states were determined at the same time and were confirmed in a series of haemodynamic and pharmacokinetic studies during continuous infusions.^{4–6}

Many strategies have been described to enable predetermined blood levels of anaesthetic and other drugs to be achieved. The simplest, a zero-order infusion, was used to achieve sedation during regional anaesthesia and in order to study the pharmacokinetics of propofol.⁶ The time taken for the blood propofol to reach a stable state exceeded an hour.

A number of complex infusion schemes have been devised based on the analyses of Wagner,⁷ Vaughan and Tucker⁸ and others, of which the BET (bolus, elimination, transfer)

scheme has been shown to be effective for other anaesthetics and analgesics.^{9–11} This scheme is based on the following premises: a loading dose (bolus) is required to fill the initial volume of distribution of the drug; a final infusion rate can be achieved which equates to the clearance (elimination) of the drug; and an interim infusion scheme is necessary to match the redistribution (transfer) of the drug from the central volume of distribution to more peripheral sites.

A computer controlled infusion system based on a three-compartment pharmacokinetic model, was designed to achieve a whole blood propofol concentration of 3.0 µg/ml within 5 minutes and to maintain it constant throughout the period of surgery. This system was tested and shown to achieve the desired blood levels.¹² An unexpected bonus was the finding that arterial pressure declined more slowly than when a single loading dose of propofol 2.5 mg/kg was given intravenously.^{5,13,14} The same infusion program was applied in a subsequent study to determine whether a pre-induction dose of fentanyl 5 µg/kg causes a pharmacokinetic interaction with propofol.¹⁵ The results of the latter study confirmed the validity of the infusion model.

Most anaesthetists do not have access to a microprocessor controller or a computer enabled volumetric infuser

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so we sought to develop a scheme which allows an anaesthetist to control a standard infusion pump in such a way as to approximate the program used by the computer controller. We present here the development and validation of such a scheme adapted for the infusion of propofol.

Methods

Our initial scheme was based on the parameters and variables of the equation which describes the three-compartment model and which would predict a desired whole blood propofol concentration (C_t) of 3.0 $\mu\text{g/kg}$:

$$C_t = Ae^{-\alpha t} + Be^{-\beta t} + Ce^{-\gamma t}$$

where A , B and C are the y -axis intercepts and α , β and γ the exponential rate constants of the relationship. The values of these parameters were derived from our own data¹⁶ and those of Gepts and colleagues⁶ based on continuous infusion of propofol. Previous schemes¹² based on pharmacokinetic data derived from single dose studies of propofol¹⁷ underestimated the initial volume of distribution of the drug and resulted in the prediction of too low a loading dose.

Figure 1 shows how a four-stage infusion scheme approximates the computer controlled infusion scheme. The manual infusion scheme was as follows: loading dose 1 mg/kg over 20 seconds; 10 mg/kg for 10 minutes; 8 mg/kg for 10 minutes; and 6 mg/kg thereafter.

Ten patients aged between 25 and 64 years who presented for superficial body surgery, who weighed 51–87 kg and were classed as ASA grade 1 or 2, were premedicated with temazepam 20–30 mg 90 minutes before operation. A 16-

gauge cannula was placed in a forearm vein for infusion of propofol from a 60-ml syringe in a Vickers Treonic IP4 infusion pump. A second 16-gauge cannula was placed in an antecubital vein in the contralateral arm for sampling of blood.

Fentanyl 3 $\mu\text{g/kg}$ was injected intravenously 2 minutes before the start of the infusion of propofol as described above. Neuromuscular blockade was achieved with vecuronium 0.1 mg/kg. The patients' tracheas were intubated and ventilation was controlled subsequently with a Penlon–Nuffield ventilator connected to a Bain system. Anaesthesia was maintained with 67% nitrous oxide in oxygen; the fresh gas flow was adjusted to maintain an end tidal carbon dioxide concentration of 5.0 kPa.

Venous blood was sampled at 2, 5, 10, 15, 20, 30, 40, 50, 60 and 80 minutes from the start of the infusion of propofol and stored at 4°C until analysis by an HPLC method with fluorometric detection.¹⁸ The electrocardiogram (CM5 lead) was displayed continuously and arterial pressures were measured immediately after each blood sample was withdrawn and at intervening 5-minute intervals with a Dinamap 845 automatic oscillotonometer.

Results

All the patients studied lost consciousness within one minute after the loading dose and the first infusion, and remained anaesthetised adequately throughout the surgical procedure. No patient complained of pain in the arm during administration of the loading dose.

The blood concentrations of propofol are shown in Table 1, and the mean values up to the first 30 minutes of

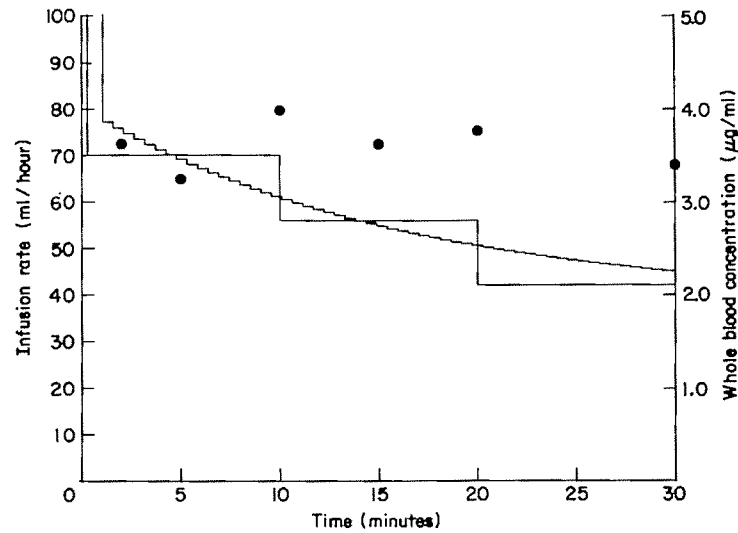


Fig. 1. Comparison of the decay of infusion rate as controlled by a computer program (small incremental steps¹²) with the three-stage manually controlled infusion, and mean whole blood propofol concentrations measured at the appropriate times. Both infusion schemes commence after the injection of 1 mg/kg as a loading dose delivered over 15–20 seconds. The present scheme underestimates the correct infusion rate in the first 5 minutes but overestimates the correct rate in the subsequent 5 minutes. These underestimates and overestimates are reflected in the blood concentrations, which are respectively lower and higher than the previous values.

Table 1. Whole blood propofol concentrations at various times from the start of infusion.

	Time, minutes									
	2	5	10	15	20	30	40	50	60	80
Mean (SD) propofol concentration, $\mu\text{g/ml}$	3.62 (1.15)	3.24 (0.83)	3.98 (0.87)	3.62 (0.74)	3.76 (0.57)	3.39 (0.55)	3.57 (0.50)	3.86 (0.57)	4.07 (0.84)	3.79 (1.04)

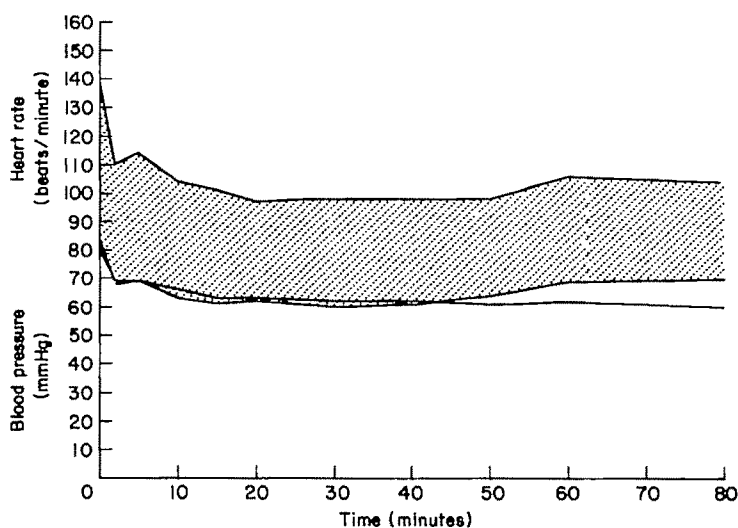


Fig. 2. Changes of systolic and diastolic arterial pressure (limits of shaded area) and heart rate during infusion of propofol.

anaesthesia are also shown in Fig. 1. The mean value at 2 minutes was slightly higher than the target value and the mean values remained consistently higher than the predicted target of $3.0 \mu\text{g/ml}$ throughout the infusion. No mean value from 5 minutes onwards differed significantly from the mean value reached at 2 minutes.

Systolic and diastolic arterial pressures and heart rate decreased slowly within the first 5 minutes (Fig. 2) but remained stable thereafter throughout the infusion. There were no significant changes of arterial pressures or heart rate in response to laryngoscopy and intubation.

Discussion

The main objective of the present study was to develop and validate a simple scheme for manual control of a propofol infusion to achieve a predetermined target concentration of propofol in blood within 2 minutes and to maintain that concentration constant for the duration of the infusion. This objective is important for a number of reasons, both for the researcher and the clinical anaesthetist. For the clinical pharmacologist there is a great advantage in the rapid attainment of a constant predetermined blood concentration of any drug. The concept was originally proposed by Kruger-Thiemer¹⁹ and subsequently by Mitenko and Ogilvie²⁰ and Wagner.⁷ The quest by anaesthetists came late and was related to the development of intravenous infusion anaesthesia.^{9-12,21,22} One of the difficulties when drug requirements for continuous infusions of intravenous anaesthesia are to be established, is that of achieving a stable blood concentration of the anaesthetic within a few minutes of the start of the infusion. With gases or volatile anaesthetics it is easy to measure the alveolar (end tidal) concentration of the agent on a breath-by-breath basis and adjust the inspired concentration so as to maintain the alveolar (and thus the blood) concentration stable. This is not feasible with intravenous anaesthetics at present so the objective can be achieved only by an infusion scheme which can be validated by retrospective measurements of the blood concentration of the relevant drug. This we have done for propofol using an open-loop computer control system¹² based on the established pharmacokinetic parameters for the drug administered as a constant infu-

sion.^{6,16} Given the weight of the patient, we can propose an infusion scheme operated by a BBC-B microcomputer and an IMED 929 computer enabled infusion pump which will achieve any desired blood propofol concentration within 2 minutes and maintain that concentration reasonably constant for the duration of anaesthesia.

The target blood concentration can be determined only by studies which define the EC_{50} and EC_{95} for a given intravenous anaesthetic under the conditions which are proposed for a specific type of surgery. For instance, the relevant values have been determined for propofol infusions to supplement 67% nitrous oxide anaesthesia in patients premedicated with lorazepam or morphine.^{2,3} From these and the empirical approaches used by many others, it is clear that a blood propofol concentration of about $3.0 \mu\text{g/ml}$ is adequate to maintain surgical anaesthesia when combined with nitrous oxide or alfentanil in a total intravenous technique.

The average clinical anaesthetist does not have access to a computer controlled system such as that described above and must therefore resort to manual control of appropriate infusion schemes. A number of schemes have been developed on empirical clinical grounds and shown to provide adequate conditions for surgery but only one, a two-bottle dilution system for methohexitone,²³ was shown consistently to provide the required blood concentration.

The method described here overcomes most of the problems previously encountered and enables a stable blood concentration to be achieved within 2 minutes of injection of the loading dose and the start of the infusion. The kinetics of propofol are linear within the range likely to be required for continuous infusions¹⁶ so higher or lower target concentrations can be achieved by a proportional increase of the four components of the scheme. The variation between patients is similar to that obtained in previous pharmacokinetic studies of propofol and represents the inherent variation which inevitably occurs when population kinetic statistics are applied for this purpose.^{24,25} The rapid attainment of the target level was achieved only after the value for the initial volume of distribution of propofol was modified according to the data derived from infusion studies^{6,16} rather than from single dose kinetic studies.¹⁷ The values for the initial volume of distribution (V_1) in the

latter study were 42.3 litres (SEM 5.9) in men and 36.1 litres (SEM 10.3) in women. If these values were used to predict the initial loading dose, there would be a 30% underestimation of the required loading dose and a failure to achieve the target blood concentration within the first 5 minutes.

One major advantage became apparent during the assessment of the computer controlled infusion¹² and during the present study: the decreases of systolic (−30 mmHg) and diastolic (−10 mmHg) arterial pressures after induction were significantly less ($p < 0.01$ and $p < 0.05$, respectively) than the decreases (systolic pressure −46 mmHg, diastolic pressure −12 mmHg) observed to follow a loading dose of 2.0 mg/kg in patients of comparable age.⁴ The decrease of systolic (−70 mmHg) and diastolic (−28 mmHg) pressures after propofol 2.0 mg/kg were even greater in an older group of patients.⁵ The peak blood propofol concentrations after an induction dose of 2.0 mg/kg can be estimated to be double those achieved in the present study, so the greater haemodynamic disturbance is hardly surprising. The blood propofol concentration achieved at 5 minutes after induction was sufficient to suppress the haemodynamic response to laryngoscopy and intubation to a greater extent than described in many other studies where the blood concentration at the time of intubation was probably lower than in the present study.^{4,5}

Acknowledgments

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References

1. PRYS-ROBERTS C, SEAR JW, ADAM HK. Pharmacokinetics of continuous infusions of Althesin, minaxolone and ICI 35,868. *British Journal of Anaesthesia* 1981; **53**: 115P.
2. SPELINA KR, COATES DP, MONK CR, PRYS-ROBERTS C, NORLEY I, TURTLE MJ. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. I. Patients premedicated with morphine. *British Journal of Anaesthesia* 1986; **58**: 1080–4.
3. TURTLE MJ, CULLEN P, PRYS-ROBERTS C, COATES DP, MONK CR, FAROQUI MH. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. II. Patients premedicated with lorazepam. *British Journal of Anaesthesia* 1987; **59**: 283–7.
4. COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE MJ. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anaesthesia in humans. *Anesthesia and Analgesia* 1987; **66**: 64–70.
5. MONK CR, COATES DP, PRYS-ROBERTS C, TURTLE MJ, SPELINA K. Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia. *British Journal of Anaesthesia* 1987; **59**: 954–60.
6. GEPTS E, CLAEYS AM, CAMU F. Pharmacokinetics of propofol (Diprivan) administered by continuous infusion in man. A preliminary report. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 51–2.
7. WAGNER JG. A safe method for rapidly achieving plasma concentrations plateaus. *Clinical Pharmacology and Therapeutics* 1974; **16**: 691–7.
8. VAUGHAN DP, TUCKER GT. General theory for rapidly establishing steady-state drug concentrations using two consecutive constant rate infusions. *European Journal of Clinical Pharmacology* 1975; **9**: 235–8.
9. SCHWILDEN H, STOECKEL H, SCHUTTLE J. Infusion strategies to investigate the pharmacokinetics and pharmacodynamics of hypnotic drugs: etomidate as an example. *European Journal of Anaesthesiology* 1985; **2**: 133–42.
10. SCHWILDEN H, STOECKEL H, SCHUTTLE J, LAUVEN PM. Interactive drug rate control in open loop systems. In: STOECKEL H, ed. *Quantitation, modelling and control in anaesthesia*. Stuttgart: Georg Thieme Verlag, 1985: 260–8.
11. LAUVEN PM, SCHWILDEN H, SCHUTTLE J. Applications of pharmacokinetic concepts in clinical anaesthesia. In: STOECKEL H, ed. *Quantitation, modelling and control in anaesthesia*. Stuttgart: Georg Thieme Verlag, 1985: 41–53.
12. TACKLEY RM, LEWIS GTR, PRYS-ROBERTS C, BOADEN RW, HARVEY JR. Open loop control of propofol infusions. *British Journal of Anaesthesia* 1987; **59**: 935P.
13. GROUNDS RM, MOORE RM, MORGAN M. The relative potencies of thiopentone and propofol. *European Journal of Anaesthesiology* 1986; **3**: 11–17.
14. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA. Dose requirements of ICI 35,868 (Propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1168–71.
15. DIXON J, LEWIS GTR, TACKLEY RM, PRYS-ROBERTS C. Fentanyl does not cause a pharmacokinetic interaction with propofol in man. *European Journal of Anaesthesiology* 1987 (in press).
16. COCKSHOTT ID, DOUGLAS EJ, PRYS-ROBERTS C, TURTLE MJ, COATES DP. Pharmacokinetics of propofol during and after i.v. infusion in man. *British Journal of Anaesthesia* 1987; **59**: 941P.
17. KAY NH, SEAR JW, UPPINGTON J, COCKSHOTT ID, DOUGLAS EJ. Disposition of propofol in patients undergoing surgery. A comparison of men and women. *British Journal of Anaesthesia* 1986; **58**: 1075–9.
18. PLUMMER GF. An improved method for the determination of Propofol (ICI 35868) in blood. *Journal of Chromatography (Biomedical Applications)* 1987; **421**: 171–6.
19. KRUGER-THEIMER E. Continuous intravenous infusion and multicompartment accumulation. *European Journal of Pharmacology* 1968; **4**: 317–22.
20. MITENKO PA, OGILVIE RI. Rapidly achieved plasma concentration plateaus with observations on theophylline kinetics. *Clinical Pharmacology and Therapeutics* 1972; **13**: 329–35.
21. SCHWILDEN H. A general method for calculating the dosage scheme in linear pharmacokinetics. *European Journal of Clinical Pharmacology* 1981; **20**: 379–86.
22. RIGG JR, WONG TY. A method for achieving rapidly steady state blood concentrations of intravenous drugs. *British Journal of Anaesthesia* 1981; **53**: 1247–57.
23. MCMURRAY TJ, ROBINSON FP, DUNDEE JW, RIDDELL JG, MCLEAN E. A method for producing constant plasma concentrations of drugs. *British Journal of Anaesthesia* 1986; **58**: 1085–90.
24. MAITRE PO, VOZEH S, HEYKANTS J, THOMSON D, STANSKI DR. Population pharmacokinetics of alfentanil: the average dose-plasma concentration relationship and interindividual variability in patients. *Anesthesiology* 1987; **66**: 3–12.
25. GREVEL J, WHITING B. The relevance of pharmacokinetics to optimal intravenous anaesthesia. *Anesthesiology* 1987; **66**: 1–2.

Infusions of propofol to supplement nitrous oxide–oxygen for the maintenance of anaesthesia

A comparison with halothane

J. W. SEAR, I. SHAW, A. WOLF AND N. H. KAY

Summary

The peri-operative and postoperative effects of propofol given by infusion were compared with halothane as a supplement to nitrous oxide–oxygen anaesthesia for body surface surgery in patients who breathed spontaneously. Anaesthesia was induced after opioid premedication, with either propofol 2.5 mg/kg or thiopentone 4–5 mg/kg which were followed respectively by an infusion of propofol 12 mg/kg/hour for 10 minutes and at a variable rate thereafter, or by halothane at a mean inspired concentration of 1.2%. Maintenance of anaesthesia required a median rate of infusion of propofol of 149.4 µg/kg/minute. The cardiovascular effects during induction and maintenance of anaesthesia were similar in the two groups. The overall incidence of side effects was low but immediate recovery was significantly faster in patients who received propofol.

Key words

Anaesthetics, gases; nitrous oxide.

Anaesthetics, intravenous; propofol.

Continuous infusion anaesthesia has been the subject of considerable recent research because of the development of intravenous hypnotic agents with appropriate pharmacokinetic profiles.^{1–3} Among the drugs studied and still clinically available are thiopentone, methohexitone, ketamine, etomidate and propofol.^{4–19} However, suggestions of hepatic enzyme abnormalities after infusions or incremental dosage regimens of thiopentone, methohexitone and ketamine,^{20–22} together with the problem and potential sequelae of adrenocortical suppression after single doses or infusions of etomidate,^{12,23} have highlighted the need for careful evaluation of the new emulsion formulation of propofol.

There are several studies in which different continuous infusion anaesthetic techniques are compared in similar groups of patients.^{19,24–26} The potential advantages of continuous infusion anaesthesia, such as minimal cardiorespiratory depression and rapid recovery, have been compared with the more conventional volatile agents.^{11,27–30} Zuurmond^{31,32} also evaluated single doses and infusions of opioids in comparison with volatile supplementation in the same group of surgical patients.

The present study compared the cardiovascular effects, quality of anaesthesia and recovery characteristics in spontaneously breathing patients who received either an infusion of propofol or halothane to supplement nitrous oxide–

oxygen for body surface surgery. An attempt was made to define the blood propofol concentrations associated with satisfactory surgical conditions.

Patients and methods

Fifty patients of ASA grade 1 or 2 about to undergo body surface surgery and who did not require neuromuscular blockade or tracheal intubation, were investigated after they had given informed consent to the study which was approved by both the Committee for Safety of Medicines and the local hospital research ethics committee. Patients were randomly allocated to receive either propofol by infusion (group P) or halothane (group H) to supplement 67% nitrous oxide in oxygen. None had clinical or laboratory evidence of hepatic or renal disease, none was receiving psychotropic drugs and none was more than 20% overweight in relation to height. Patients in whom the use of halothane was clinically contraindicated were excluded from the study.

Patients were premedicated with papaveretum 10–20 mg and hyoscine 0.2–0.4 mg intramuscularly one hour before induction of anaesthesia. Sleep was induced with propofol 2.5 mg/kg (group P) or thiopentone 4–5 mg/kg (group H). Anaesthesia in the former group was maintained with an infusion of propofol to supplement nitrous oxide; in the

Table 1. Demographic details, duration of anaesthesia and total dose of propofol in groups P and H. Values expressed as mean (SD) or number of patients, as appropriate.

	Age, years	Weight, kg	Sex, M/F	Duration of anaesthesia, minutes	Dose of propofol, mg
Group P (<i>n</i> = 25)	42.4 (11.5)	67.4 (11.1)	12/13	38.4 (15.2)	559.0 (176.7)
Group H (<i>n</i> = 25)	42.3 (11.5)	64.2 (10.7)	6/19	37.1 (18.4)	—

No significant differences between groups.

latter, with 1–2% halothane. The patients breathed spontaneously via a Lack breathing system and facemask. The infusion of propofol (group P) was set at an initial rate of 12 mg/kg/hour for 10 minutes, then decreased to 9 mg/kg/hour and adjusted thereafter according to the clinical needs of the patient. The infusion of propofol was stopped about 5 minutes before the end of the surgical procedure.

The duration of anaesthesia (to cessation of nitrous oxide) was noted. Two indices of immediate recovery were recorded by a blinded observer: the time from cessation of nitrous oxide until patients opened their eyes on command, and the interval before the correct date of birth was given on request. In addition, recovery performance over the first postoperative hour was assessed using the modified Steward's score.³³

Side effects or adverse effects that occurred during induction, maintenance or recovery from anaesthesia were recorded, especially those related to pain during induction of anaesthesia, venous sequelae in the first 24 hours after anaesthesia (phlebitis, thrombosis) and the presence of awareness. An overall global assessment was made by the anaesthetist in charge of the case, of the quality of anaesthesia as well as the ease of control of depth of anaesthesia.

The electrocardiogram and heart rate during the operative period were monitored continuously using leads in the CM₅ configuration. Arterial systolic and diastolic blood pressures were recorded during induction of anaesthesia and at 5-minute intervals thereafter using a Copal automatic arterial blood pressure recorder (Copal Digital Sphygmomanometer, UA-251).

Blood samples (5 ml into tubes containing potassium oxalate) were taken in patients in group P to estimate propofol concentrations at surgical incision, at times of inadequate anaesthesia (i.e. acute movements during surgery) and at the end of the infusion of propofol. The samples were stored at 4°C until assay by high-performance liquid chromatography for whole blood concentrations after extraction into cyclohexane. Detection of drug concentrations was by a fluorescence technique. The limit of sensitivity of the assay was 5 ng/ml and the coefficient of variation approximately 8% over the observed concentration range.

Statistical analysis. Demographic details and duration of anaesthesia were compared using Student's unpaired *t*-test. Recovery times were subjected to logarithmic transformation to correct for positive skewness and then compared similarly. The incidence of side effects within the two treatment groups was compared by Fisher's exact test or the Chi-squared test with Yates' correction for small samples. Comparison of cardiovascular parameters was by Friedman two-way analysis of variance and the sign test. Blood propofol concentrations at incision and at the end of infusion were calculated as the mean and standard deviation, and the relationship between the concentration at the end of the infusion and recovery compared using the Spearman rank correlation test. The average infusion rate

of propofol was calculated as the total dose (including the induction dose) divided by the duration of infusion. The average maintenance rate was defined as the total dose minus the induction dose and the initial fast phase infusion dose, divided by the duration of the infusion.

Results

Fifty patients (18 male) aged 16–64 years and of weight 49.5–98.3 kg were studied, of whom 25 received propofol. The demographic details, total drug doses and durations of anaesthesia in the two groups are shown in Table 1.

Onset of unconsciousness occurred 24.0 seconds (SD 7.1) after the start of injection in group P and at 23.8 seconds (7.3) in group H. The median infusion rate in group P was 221.9 µg/kg/minute (range 139.0–321.1) and the median maintenance rate 149.4 µg/kg/minute (range 83.8–201.3). There was no correlation between the propofol maintenance rate and patient weight or the duration of anaesthesia. There was no difference in the median rate between male and female patients in group P (female (*n* = 13), 149.4 µg/kg/minute; male (*n* = 12), 146.3 µg/kg/minute). Anaesthesia in group H was maintained with an average inspired halothane concentration of 1.2%.

The cardiovascular responses to anaesthesia and surgery are shown in Fig. 1. Induction of anaesthesia in group P resulted in a maximum decrease in systolic arterial blood pressure over the first 10 minutes of 21.5%, and of 16% in diastolic pressure (*p* = 0.001, *p* = 0.006). The peak increase in heart rate was 12%, which was not significant. In contrast, group H showed a 21.5% increase in heart rate (*p* = 0.001) and 25.4% and 14.5% maximum decreases in systolic and diastolic arterial pressure, respectively (*p* = 0.001, *p* = 0.002). The maximum response to surgical incision in group H, +13.2%, +7.5% and +11.6%, respectively for systolic, diastolic arterial pressure and heart rate (*p* = 0.001, 0.01 and 0.05 versus values before incision), was greater than the corresponding values of +2.2%, +4.2% and –6.0% in group P, none of which was statistically significant. Five patients in group H required atropine for heart rates < 40 beats/minute coupled with hypotension. The haemodynamic values in both groups of patients at the end of surgery were not clinically different from those before induction.

The incidence of other untoward effects during induction and maintenance of anaesthesia is shown in Table 2. No patient had postoperative venous sequelae. Induction was scored as good or adequate in 45 out of 50 patients, and 49 out of 50 scored similarly for maintenance of anaesthesia. There were four poor induction sequences in group P which were related to light anaesthesia, involuntary movement after induction and hypertonus in the period prior to incision. One of these patients received fentanyl 50 µg as a supplement to the infusion. The patient with poor maintenance was also in group P and experienced alter-

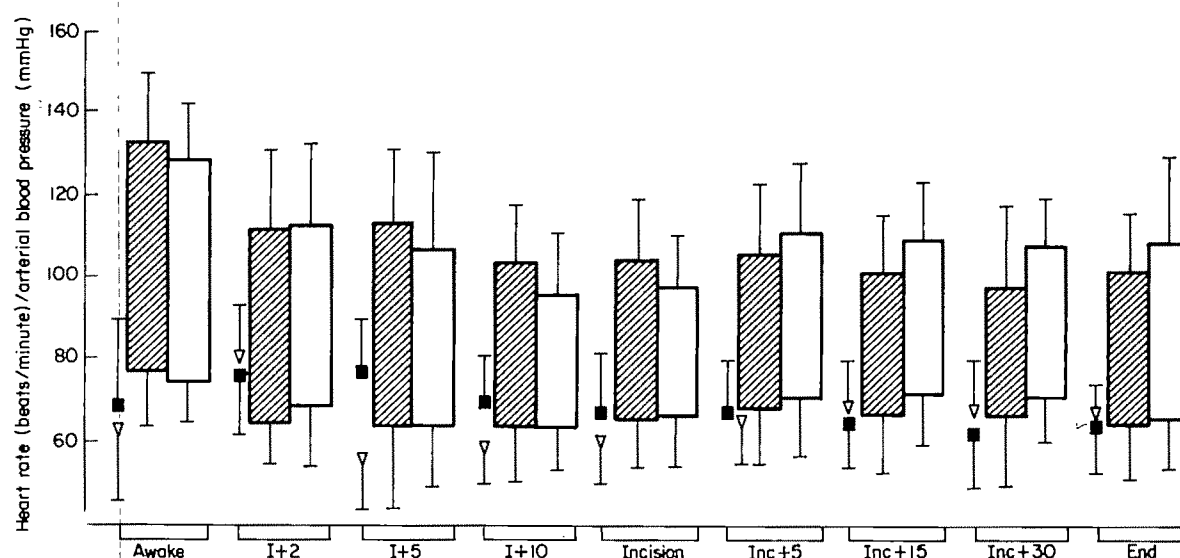


Fig. 1. Haemodynamic responses to induction of anaesthesia and to surgical incision in patients who received either propofol (group P) or halothane (group H) to supplement 67% nitrous oxide in oxygen. Data shown as mean (SD). \square , Arterial blood pressure, \blacksquare , heart rate in group P; \square , arterial pressure, ∇ , heart rate in group H. I, times after induction of anaesthesia (minutes); Inc, times after surgical incision (minutes).

Table 2. Incidence of side effects during induction, maintenance and early recovery from anaesthesia. Values expressed as numbers of patients.

	Group P	Group H	
<i>During induction</i>			
Pain on injection	5	0	$p = 0.025$
Excitatory phenomena	4	0	$p = 0.055$
Apnoea > 30 seconds	10	9	NS
Cough, respiratory upsets	1	3	NS
<i>During maintenance</i>			
Movement on surgical stimulus	12	4	$p = 0.03$
Intra-operative bradycardia	0	5	$p = 0.025$
Cardiac dysrhythmias	1	2	NS
<i>Recovery</i>			
Greater than 20 minutes to giving date of birth	8	15	$p = 0.05$
Restlessness	0	3	NS

NS, Not significant.

Table 3. Recovery times and percentage of patients who achieved a Steward recovery score of 6 at 3, 10, 20 and 30 minutes after the end of nitrous oxide administration.

	Group P	Group H	
<i>Time to opening eyes,* minutes</i>			
	12.0	17.8	$p = 0.02$
95% confidence limits	(9.7–14.8)	(14.2–22.2)	
<i>Time to giving date of birth,* minutes</i>			
	18.8	25.3	$p = 0.05$
95% confidence limits	(15.6–22.6)	(20.5–31.3)	
<i>Steward score of 6</i>			
3 minutes	0%	0%	NS
10 minutes	4%	4%	NS
20 minutes	52%	24%	$p = 0.05$
30 minutes	88%	52%	$p = 0.02$

NS, Not significant.

* Values are geometric means.

nating episodes of intra-operative apnoea and inadequate anaesthesia.

The times to open eyes to command and to correct response (date of birth) were significantly less in group P ($p < 0.02$ and $p < 0.05$, respectively) (Table 3). Comparison of the Steward modified recovery scores showed significantly faster attainment of a score of 6 in group P.

Figure 2 shows the blood propofol concentrations at surgical incision, at times of inadequate anaesthesia and at the end of the infusion. The average propofol concentration at incision was $4.93 \mu\text{g/ml}$ (SD 1.51). Satisfactory clinical anaesthesia was achieved at propofol concentrations greater than $3.0 \mu\text{g/ml}$. The mean concentration at the end of the propofol infusion was $3.35 \mu\text{g/ml}$ (SD 1.50). No correlation existed between the propofol concentration at the end of infusion and the achievement of any index of immediate recovery. None of the patients reported awareness during anaesthesia, including those who responded to the surgical stimulus.

Discussion

Our previous study in which incremental doses of propofol were used to supplement nitrous oxide–oxygen, showed that propofol provides satisfactory anaesthesia with rapid and complete recovery.²⁷ However, the constantly changing drug concentration during incremental dosage results in periods of light anaesthesia followed by periods of excessive neurophysiological suppression. The data presented here demonstrate that a variable rate infusion technique^{19,34,35} provides stable anaesthesia in the spontaneously breathing patient who receives propofol. The incidence of patient movement in response to surgery was greater than in the thiopentone–halothane group but this probably represents a lower state on the learning curve for this new agent.

Various approaches have been used to achieve stable blood drug concentrations more rapidly.³ Propofol has a large steady-state volume of distribution (4.8 litres/kg).³⁶ The loading dose given prior to a continuous infusion in order to facilitate the achievement of steady drug con-

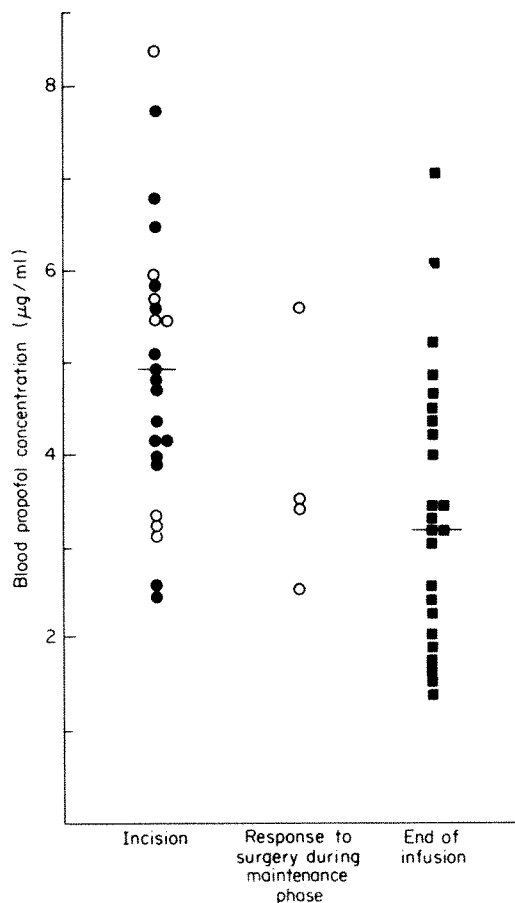


Fig. 2. Blood propofol concentrations in patients in group P. Points represent individual values in 24 patients at the times shown. The bars indicate mean propofol concentrations. Propofol concentrations were not available for one patient in the group. ○, Response; ●, no response.

centrations is best administered, in fit ASA grade 1 or 2 patients, as a single induction dose of 2.5 mg/kg and an initial rapid phase infusion (12 mg/kg/hour) because of the pronounced dose-related cardiovascular depressant effects of the agent. This regimen, followed by the maintenance rate of 9 mg/kg/hour, was based on a pilot study (Wolf and Kay, unpublished observations).

The range of maintenance infusion rates was similar to that in our earlier study²⁷ and the average infusion rate was comparable to those reported in other patients who received propofol to supplement nitrous oxide-oxygen.^{19,25,26,28-30,34,35,37} The rates were, however, in excess of those described by Spelina¹⁷ for the MIR (minimum infusion rate) in comparable opioid premedicated patients. The MIR is by definition an ED₅₀ rate and higher infusion rates (e.g. ED₉₅) are employed in clinical practice. There was no difference between our median rate and the ED₉₅ of Spelina (112.2 µg/kg/minute, 95% confidence limits 85.6-306.2).

The haemodynamic changes during infusion of propofol were similar to those in the halothane group, although propofol appeared to be associated with slower heart rates and differs therefore from infusions of methohexitone^{8,16,19,25,34} which are associated with a significant tachycardia at comparable infusion rates. The incidence of side effects was low in both groups. Propofol was also associated with significantly shorter times to awakening

and orientation, and with a low incidence of postoperative complications. The lack of correlation between propofol concentrations at the end of the infusion and time to recovery may appear surprising. However, the condition was not stable since there were different surgical incisions and thus different degrees of postoperative pain. The absence of a relationship between the total dose of propofol and the indices of recovery agrees with previous data.^{17,27}

Propofol concentrations at incision were similar to the IC₉₅ value reported by Spelina and colleagues¹⁷ and agree well with the data of Van Doze.¹⁹ The wide range of concentrations associated with patient response must cast doubts on the rationale for fixed infusion regimens rather than on infusion rate that is varied according to clinical need.

Our data show that propofol in opioid premedicated patients provides induction and maintenance of anaesthesia with similar efficacy and safety to that achieved with thiopentone-halothane. The incidence of pain on injection of propofol was less than in the previous incremental dose study but the occurrence of apnoea was comparable. Recovery from anaesthesia in this study was not as prompt as in the study of Kay,²⁷ which reflects the higher infusion rates in the present patients. Further investigation might involve use of a lower maintenance infusion, again varied according to clinical needs. The present data suggest that propofol is a suitable agent for continuous infusion anaesthesia in the spontaneously breathing patient, and that it provides easy control of the depth of anaesthesia with good surgical conditions and recovery characteristics.

References

- MORGAN M. Total intravenous anaesthesia. *Anaesthesia* 1983; **38** (Suppl.): 1-9.
- SEAR JW. General kinetic and dynamic principles and their application to continuous infusion anaesthesia. *Anaesthesia* 1983; **38** (Suppl.): 10-25.
- STANSKI DR. The role of pharmacokinetics in anaesthesia: application to intravenous infusions. *Anaesthesia and Intensive Care* 1987; **15**: 7-14.
- HUNTER AR. Thiopentone supplemented anaesthesia for neurosurgery. *British Journal of Anaesthesia* 1972; **44**: 506-10.
- WHITE PF. Continuous infusions of thiopental, methohexital or etomidate as adjuvants to nitrous oxide for outpatient anaesthesia. *Anesthesia and Analgesia* 1984; **63**: 282.
- CRANKSHAW DP, EDWARDS NE, BLACKMAN GL, BOYD MD, CHAN HNJ, MORGAN DJ. Evaluation of infusion regimens for thiopentone as a primary anaesthetic agent. *European Journal of Clinical Pharmacology* 1985; **28**: 543-52.
- TODD MM, DRUMMOND JC, HOI SANG U. The hemodynamic consequences of high-dose methohexital anaesthesia in humans. *Anesthesiology* 1984; **61**: 495-501.
- PRYS-ROBERTS C, SEAR JW, LOW JM, PHILLIPS KC, DAGNINO J. Hemodynamic and hepatic effects of methohexital infusion during nitrous oxide anaesthesia in humans. *Anesthesia and Analgesia* 1983; **62**: 317-23.
- MAGNUSSON H, PONTÉN J, SONANDER HG. Methohexitone anaesthesia for micro-laryngoscopy: circulatory modulation with metoprolol and dihydralazine. *British Journal of Anaesthesia* 1986; **58**: 976-82.
- LILBURN JK, DUNDEE JW, MOORE J. Ketamine infusions. Observations on technique, dosage and cardiovascular effects. *Anaesthesia* 1978; **33**: 315-21.
- LEES NW, ANTONIOS WRA. Two stage infusion of etomidate for the induction and maintenance of anaesthesia. *British Journal of Anaesthesia* 1984; **56**: 1239-42.
- MOORE RA, ALLEN MC, WOOD PJ, REES LH, SEAR JW. Peri-operative endocrine effects of etomidate. *Anaesthesia* 1985; **40**: 124-30.



13. MAJOR E, VERNIQUET AJW, WADDELL TK, SAVEGE TM, HOFFLER DE, AVELING W. A study of three doses of ICI 35868 for induction and maintenance of anaesthesia. *British Journal of Anaesthesia* 1981; **53**: 267-72.
14. MAJOR E, VERNIQUET AJW, YATE PM, WADDELL TK. Disopropofol and fentanyl for total intravenous anaesthesia. *Anaesthesia* 1982; **37**: 541-7.
15. O'CALLAGHAN AC, NORMANDALLE JP, GRUNDY EM, LUMLEY J, MORGAN M. Continuous intravenous infusion of disopropofol (ICI 35868, Diprivan). Comparison with Althesin to cover surgery under local analgesia. *Anaesthesia* 1982; **37**: 295-300.
16. PRYS-ROBERTS C, DAVIES JR, CALVERLEY RK, GOODMAN NW. Haemodynamic effects of infusions of diisopropyl phenol (ICI 35868) during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1983; **55**: 105-11.
17. SPELINA KR, COATES DP, MONK CR, PRYS-ROBERTS C, NORLEY I, TURTLE MJ. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. I. Patients premedicated with morphine sulphate. *British Journal of Anaesthesia* 1986; **58**: 1080-4.
18. HILTON P, DEV VJ, MAJOR E. Intravenous anaesthesia with propofol and alfentanil. The influence of age and weight. *Anaesthesia* 1986; **41**: 640-3.
19. DOZE VA, WESTPHAL LM, WHITE PF. Comparison of propofol with methohexital for outpatient anaesthesia. *Anesthesia and Analgesia* 1986; **65**: 1189-95.
20. DUNDEE JW. Thiopentone as a factor in the production of liver dysfunction. *British Journal of Anaesthesia* 1955; **27**: 14-23.
21. BITTRICH NM, KANE AV, MOSHER RE. Methohexital and its effects on liver function tests. *Anesthesiology* 1963; **24**: 81-90.
22. DUNDEE JW, FEE JPH, MOORE J, MCILROY PDA, WILSON DB. Changes in serum enzymes following ketamine infusions. *Anaesthesia* 1980; **35**: 12-16.
23. ZURICK AM, SIGURDSSON H, KOEHLER LS, GHATTAS MA, SEITHNA DH, ROBERTS MM, ESTAFANOUS PG. Increased post-operative respiratory morbidity with a single dose of etomidate. *Critical Care Medicine* 1986; **14**: 322.
24. DE GROOD PMRM, HARBERS JBM, VAN EGMOND J, CRUL JF. Anaesthesia for laparoscopy. A comparison of five techniques including propofol, etomidate, thiopentone and isoflurane. *Anaesthesia* 1987; **42**: 815-23.
25. SAMPSON IH, LEFKOWITZ M, COHEN M, MIKULA S, KAPLAN JA. A comparison of propofol and methohexital for anaesthesia by continuous infusion. *Anesthesia and Analgesia* 1987; **66**: S150.
26. WEINGARTEN M. Propofol versus thiopentone for induction and maintenance of general anaesthesia for brief surgical procedures. *Canadian Journal of Anaesthesia* 1987; **34**: S79.
27. KAY NH, UPPINGTON J, SEAR JW, ALLEN MC. Use of an emulsion of ICI 35868 (propofol) for the induction and maintenance of anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 736-42.
28. VINIK HR, SHAW B, MACKRELL T, HUGHES G. A comparative evaluation of propofol for the induction and maintenance of general anaesthesia. *Anesthesia and Analgesia* 1987; **66**: S184.
29. YOUNGBERG JA, TEXIDOR MS, SMITH DE. A comparison of induction and maintenance of anaesthesia with propofol to induction with thiopental and maintenance with isoflurane. *Anesthesia and Analgesia* 1987; **66**: S191.
30. ZUURMOND WWA, VAN LEEUWEN L, HELMERS JHJH. Recovery from propofol infusion as the main agent for outpatient arthroscopy. A comparison with isoflurane. *Anaesthesia* 1987; **42**: 356-9.
31. ZUURMOND WWA, VAN LEEUWEN K. Alfentanil v. isoflurane for outpatient arthroscopy. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 329-31.
32. ZUURMOND WWA, VAN LEEUWEN L. Recovery from sufentanil anaesthesia for outpatient arthroscopy: a comparison with isoflurane. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 154-6.
33. STEWARD DJ. A simplified scoring system for the postoperative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-3.
34. MACKENZIE N, GRANT IS. Propofol (Diprivan) for continuous intravenous anaesthesia. A comparison with methohexital. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 70-5.
35. DOZE VA, WHITE PF. Comparison of propofol with thiopental-isoflurane for induction and maintenance of outpatient anaesthesia. *Anesthesiology* 1986; **65**: A544.
36. KAY NH, SEAR JW, UPPINGTON J, COCKSHOTT ID, DOUGLAS EJ. Disposition of propofol in patients undergoing surgery: a comparison in men and women. *British Journal of Anaesthesia* 1986; **58**: 1075-9.
37. HERREGODS L, ROLLY G, VERSICHELEN L, ROSSEEL MT. Propofol combined with nitrous oxide-oxygen for induction and maintenance of anaesthesia. *Anaesthesia* 1987; **42**: 360-5.

Pharmacokinetics of propofol administered by continuous infusion in patients with cirrhosis

Preliminary results

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C. WINCKLER

Summary

Anaesthesia was provided by an infusion of propofol in six healthy patients and six patients with hepatic cirrhosis. There were no significant differences between the groups with regard to the central compartment volume, distribution volume at steady state, total apparent distribution volume, total body clearance or elimination half-life, although the values were always greater in the cirrhotic patients. Recovery times were significantly longer in the patients with cirrhosis.

Key words

Anaesthetics, intravenous; propofol.

Complications; hepatic cirrhosis.

Propofol is suitable for maintenance of anaesthesia by continuous infusion. No difference in the pharmacokinetic behaviour of propofol was observed after a single bolus injection in patients with cirrhosis of the liver and in healthy subjects¹ despite extensive hepatic metabolism. However, the pharmacokinetics of propofol might be affected by the presence of cirrhosis when prolonged infusions are used.

The present study was designed to investigate the pharmacokinetics of propofol administered by infusion for a minimum of 2 hours in patients with cirrhosis. Data were compared with those from healthy subjects.

Methods

Six patients with histologically proven cirrhosis of the liver, of mean age 54 years (SEM 10) and who weighed 64 kg (SEM 9) were studied. Six patients without hepatic or renal alteration, mean age 37 years (SEM 16) and mean weight 63 kg (SEM 16), served as controls. All patients had elective nonhaemorrhagic surgery. Patients with cirrhosis were classified as A or B according to Child's criteria.

Premedication consisted of diazepam 10 mg orally and atropine 0.5 mg intramuscularly. After injection of fentanyl 100 µg, a propofol infusion was started at a rate of 21 mg/kg/hour for 5 minutes. The rate was then reduced to 12 mg/kg/hour for 10 minutes and subsequently maintained at 6 mg/kg/hour. Orotracheal intubation was achieved after administration of pancuronium. Ventilation was mechanically controlled using a nitrous oxide and oxygen mixture. Supplements of fentanyl were given as required. The propo-

fol infusion was stopped at the end of the surgical procedure.

Serial samples of whole blood were taken during the infusion and up to 8 hours after the end of the infusion to determine propofol levels by high-performance liquid chromatography. Pharmacokinetic analysis of data obtained after the end of the infusion was performed with a nonlinear least-squares regression programme. The following parameters were derived: central compartment volume, distribution volume at steady state, total apparent distribution volume, total body clearance and elimination half-life (t_1). Recovery was measured as the time when patients opened their eyes on command and answered questions correctly. The significance of observed differences between patient groups was assessed by the Wilcoxon rank sum test.

Results

Pharmacokinetic parameters are shown in Table 1. There were no significant differences between the control and cirrhotic groups for any of the parameters estimated. However, the times until patients could open their eyes on command and answer questions correctly were significantly longer in patients with cirrhosis than in healthy patients: 38 minutes (SD 34) versus 17 minutes (SD 5) and 57 minutes (SD 45) versus 30 minutes (SD 8), respectively. The mean total dose of fentanyl given as supplement was 270 µg (SD 225) in cirrhotic patients and 460 µg (SD 240) in healthy subjects. The mean propofol concentration at the time of recovery did not differ between cirrhotic and healthy patients

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Table 1. Pharmacokinetic parameters. Values expressed as mean (SD).

	Normal (n = 6)	Cirrhosis (n = 6)
Central compartment volume, litres	137 (49)	234 (153)
Distribution volume at steady state, litres	546 (169)	637 (349)
Total apparent distribution volume, litres	730 (239)	858 (427)
Total body clearance, litres/minutes	2.10 (0.42)	2.17 (0.64)
Elimination half-life, minutes	222 (66)	266 (92)

(0.9 µg/ml (SD 0.5) versus 1.1 µg/ml (SD 0.5), respectively).

Discussion

The pharmacokinetics of propofol after prolonged infusion were similar in both patient groups, as for a single bolus injection. The central compartment volume was slightly increased in patients with cirrhosis. Clearance values for most individuals in both groups are higher than the estimate of normal hepatic blood flow (1.5 litres/minute). Consequently, extrahepatic sites of metabolism for propofol are likely to be involved and may counterbalance the decrease in hepatic blood flow commonly associated with cirrhosis.

This alternative mechanism could explain the absence of any difference in total body clearance between the two groups. Patients with cirrhosis showed no major alterations in pharmacokinetics but recovery was slower than in healthy patients. An increased sensitivity in patients with cirrhosis may be eliminated since the blood concentrations of propofol measured at the time of recovery were similar in the two groups.

Reference

1. SERVIN F, HABERER JP, COCKSHOT ID, FARINOTTI R, DESMONTS JM. Propofol pharmacokinetics in patients with cirrhosis *Anesthesiology* 1986; **65**: A554.

Effects of propofol on cardiovascular dynamics and coronary blood flow in geriatric patients

A comparison with etomidate

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Summary

The cardiovascular and myocardial effects of propofol and etomidate were studied in 20 geriatric patients (age 65–84 years) who underwent major upper abdominal surgery. Ten patients received propofol 1.5 mg/kg for induction of anaesthesia followed by a continuous infusion of 0.1 mg/kg/minute for maintenance; 10 patients received etomidate 18 mg for induction followed by 2.4 mg/minute for maintenance. Vecuronium was used for neuromuscular blockade. Cardiovascular dynamics were recorded in the awake state one minute after induction and 1, 5 and 30 minutes after tracheal intubation; coronary blood flow (argon wash-in) and myocardial oxygen consumption were determined in the awake state and 5 and 30 minutes after intubation. Both anaesthetics decreased systolic, diastolic and mean arterial pressures, heart rate and cardiac index to the same extent. Myocardial blood flow and oxygen consumption were also reduced in both groups due to a reduction in cardiac work. Tracheal intubation produced a marked increase in arterial pressure in the etomidate group, while haemodynamic changes were absent in the propofol group. Myocardial lactate production was not observed in either group 5 or 30 minutes after tracheal intubation.

Key words

Anaesthesia; geriatric.

Anaesthetics, intravenous; propofol, etomidate.

Cardiovascular reserve is diminished in old age and requires careful selection of anaesthetics to avoid undue depression of cardiac and circulatory function. Etomidate produces only minimal effects on cardiovascular and coronary dynamics in healthy subjects¹ and is therefore widely employed in geriatric anaesthesia and in patients with cardiovascular disease. However, the drug has been shown not to attenuate cardiovascular responses to noxious stimulation reliably in a definite percentage of surgical patients, which limits its usefulness in geriatric patients. Propofol, on the other hand causes a uniform decrease in mean arterial pressure which appears to be dose related and is more pronounced in patients with valvular or coronary heart disease,^{2–4} while haemodynamic changes after tracheal intubation or sternotomy seem to be largely prevented.^{3,4} This study was designed to compare the cardiovascular and myocardial effects of propofol with etomidate in elderly patients without clinical manifestations of heart failure or coronary artery disease.

Methods

The study was approved by the Göttingen University Human Subjects Review Committee and written informed consent was given by all patients. The patients were 65

years of age or more and were scheduled to undergo major upper abdominal surgery. Those with signs and symptoms of heart failure, valvular or ischaemic heart disease or severe systemic disease were not studied. Hypertensive subjects received their last antihypertensive medication on the evening before operation. Twenty patients were studied and were randomly allocated into two equal groups (propofol and etomidate). All were premedicated with piritramide 7.5 mg and promethazine 25 mg intramuscularly one hour before arrival in the anaesthetic room.

A three-lead electrocardiograph was attached on arrival in the anaesthetic room and the trace obtained was displayed continuously on a Hellige patient monitor. The following catheters were inserted percutaneously under local anaesthesia: a Goodale–Lubin catheter (7F, USCI) into the coronary sinus via the right internal jugular vein for measurement of coronary blood flow and withdrawal of blood samples; a second Goodale–Lubin catheter (7F, USCI) into the nondominant radial artery for continuous monitoring of arterial blood pressure and blood sampling; a flow-directed pulmonary artery catheter (Vygon quadruple thermodilution Thermocath) via a left or right antecubital vein for measurement of pulmonary artery pressure, pulmonary artery wedge pressure, right atrial pressure and cardiac output; a polyurethane catheter into the superior vena cava

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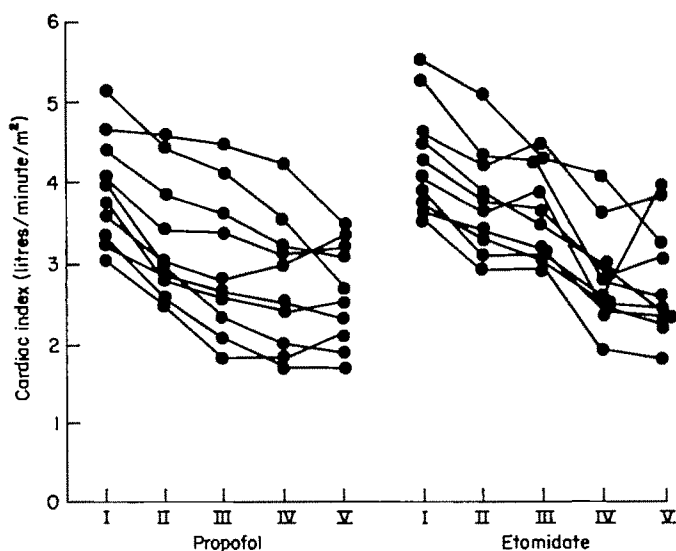


Fig. 1. Changes in cardiac index. Single values of 20 patients. I, Awake; II, lowest value after induction; III, highest value after intubation; IV, V, 5 and 30 minutes after intubation. No significant difference between groups.

Table 1. Details of patients.

	Propofol group (n = 10)	Etomidate group (n = 10)
Total	10	10
Sex, M/F	4/6	3/7
Mean (SD) age, years	73(6)	73(6)
Range	65–82	65–82
Mean (SD) weight, kg	63.9 (12)	62(8)
Range	40–75	51–73
Hypertensive (treated)	6	6

for administration of drugs; and a 13-gauge venous cannula in a peripheral vein for administration of fluids. The position of all catheters was confirmed by fluoroscopy. The systemic arterial, pulmonary arterial and central venous pressures were displayed continuously on the patient monitor and simultaneously recorded on a 10-channel chart recorder (Hellige); together with the beat-to-beat heart rate. All patients received 750–1000 ml of a balanced electrolyte solution during insertion of catheters and the resting period.

Myocardial blood flow (MBF) was measured by the argon wash-in technique⁵ with blood sampled from the coronary sinus and the radial artery during inhalation of a standard concentration of argon in oxygen. Cardiac output was measured by the thermodilution technique using 10 ml of saline solution at 0°C (cardiac output computer, Fischer BN 7206); the arithmetic mean of three consecutive values was taken. Measurements of cardiac output and wedge pressure were performed at the end of expiration. Samples were taken simultaneously from the coronary sinus and the radial artery before and after each measurement of myocardial blood flow, and analysed for PO_2 , PCO_2 , pH, base excess and standard bicarbonate (IL 282, Instrumentation Laboratories), haemoglobin concentration and oxygen saturation (Co-oximeter IL 282, Instrumentation Laboratories), and electrolyte concentrations by flame photometry (IL 543, Instrumentation Laboratories) and lactate (standard test combination, Boehringer).

Fentanyl 0.1 mg was injected during pre-oxygenation following baseline measurements after 30 minutes of rest,

and anaesthesia was induced thereafter with either propofol 1.5 mg/kg followed by continuous infusion of 0.1 mg/kg/minute or by etomidate 18 mg followed by continuous infusion of 2.4 mg/minute. Vecuronium 0.1 mg/kg was administered to facilitate tracheal intubation. Further haemodynamic measurements were made 1–2 minutes after induction (ventilation was not assisted), during controlled normoventilation with oxygen at the peak of the haemodynamic response after laryngoscopy and immediate tracheal intubation, and 5 and 30 minutes after completion of tracheal intubation. Myocardial blood flow and myocardial oxygen consumption were determined in the awake state, 5 minutes after tracheal intubation and 30 minutes after intubation only, for methodological reasons, since 15 minutes between measurements are required for desaturation of the body from argon.

Systemic and pulmonary vascular resistances, stroke volume index and cardiac index were calculated using standard formulae. Coronary vascular resistance was determined as mean arterial pressure – pulmonary artery wedge pressure divided by myocardial blood flow. Myocardial oxygen consumption was calculated by multiplying arterial–coronary sinus blood oxygen content difference by myocardial blood flow.

Statistical analysis of the data was by sign test and by median test; $p < 0.05$ was assigned statistical significance.

Results

Patients ranged in age from 65 to 82 years in both groups. There were no significant differences between the two groups in age and weight (Table 1) or in cardiovascular variables. Six patients in each group were known to be hypertensive and received maintenance doses of anti-hypertensive agents but had no signs and symptoms of hypertensive heart disease. Systolic blood pressure of these patients was elevated (above 160 mmHg) on arrival in the anaesthetic room and remained so even after a resting period of 30 minutes, while diastolic pressure was in the normal range. Baseline cardiac index was in the upper range or slightly elevated in half of the patients (Fig. 1); myocardial blood flow and myocardial oxygen consumption

Table 2. Cardiovascular data. Values expressed as mean (SD).

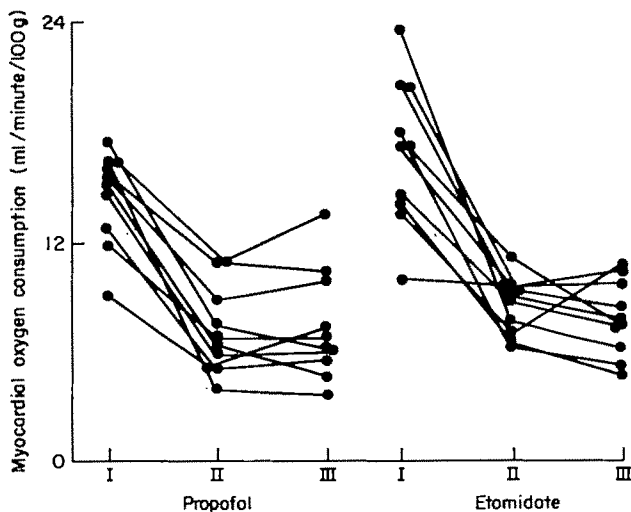
	Awake	Lowest after induction	Highest after intubation	5 minutes after intubation	30 minutes after intubation
Heart rate, beats/minute	P 70(10) E 81(14)	66(8) 74(15)*	64(12) 75(13)*	62(12)* 66(14)*	58(8)* 61(13)*
Systolic arterial pressure, mmHg	P 177(37) E 172(21)	120(20)* 147(19)*	123(43)*† 186(27)	111(27)* 110(15)*	107(17)* 109(18)*
Diastolic arterial pressure, mmHg	P 74(8) E 80(9)	54(7)* 68(13)*	55(15)*† 93(21)	54(11)* 59(11)*	53(9)* 58(12)*
Mean arterial pressure, mmHg	P 111(17) E 116(13)	74(12)* (95)14*	77(25)*† 124(26)*	73(20)* 78(13)*	72(10)* 75(16)*
Mean pulmonary arterial pressure, mmHg	P 20(5) E 20(5)	16(5)* 17(7)	18(5) 21(5)	17(5) 14(5)*	14(3)* 14(5)*
Mean pulmonary capillary wedge pressure, mmHg	P 11(4) E 9(3)	9(4)* 9(4)	9(3) 10(4)	9(3) 8(3)	8(2) 8(4)
Central venous pressure, mmHg	P 3(2) E 3(2)	3(2) 4(3)	4(2) 4(3)	4(2) 3(3)	4(2) 3(3)
Cardiac index, litres/minute/sq m	P 4.01(0.6) E 4.38(0.6)	3.3(0.8)* 3.7(0.7)*	2.85(0.7)* 3.65(0.6)*	2.76(0.8)* 2.79(0.6)*	2.65(0.6)* 2.78(0.7)*
Stroke volume index, ml/sq m	P 56(7) E 54(6)	50(7)* 50(6)*	47(8)* 49(7)*	45(8)* 43(7)*	44(8)* 46(9)
Systemic vascular resistance, dyne s/cm ⁵	P 1371(440) E 1293(354)	1133(388)* 1209(308)	1460(532) 1605(333)	1231(374) 1336(263)	1232(375) 1344(299)
Pulmonary vascular resistance, dyne s/cm ⁵	P 106(25) E 131(39)	102(44) 129(59)	171(33)* 143(47)	139(52)* 116(39)	105(33) 118(47)

P, Propofol; E, Etomidate.

* $p < 0.05$, awake versus other data; † $p < 0.05$, propofol versus etomidate.**Table 3.** Myocardial data. Values expressed as mean (SD).

	Awake	5 minutes after intubation	30 minutes after intubation
Myocardial blood flow, ml/minute/100 g	P 142(20) E 145(34)	86(25)* 75(19)*	95(37)* 75(21)*
Myocardial oxygen consumption, ml/minute/100 g	P 15.2(1.8) E 16.1(4.7)	7.5(2.2)* 8.5(1.6)*	8.1(2.9)* 7.7(2)*
Coronary vascular resistance, mmHg/ml/minute/100 g	P 0.71(0.2) E 0.67(0.2)	0.81(0.2) 1.00(0.5)	0.85(0.3) 0.86(0.4)
Arterial-coronary sinus blood oxygen content difference, vol. %	P 10.1(1.9) E 11.2(2.4)	9.0(1.9)* 10.3(1.8)	8.8(1.4)* 9.1(1.6)*
Coronary sinus blood oxygen saturation, %	P 32.8(7) E 29.1(6)	39.9(6)*† 35.7(5)*	39.9(5)* 39.1(6)*

P, Propofol; E, Etomidate.

* $p < 0.05$, awake versus other data; † $p < 0.01$; propofol versus etomidate.**Fig. 2.** Changes in myocardial oxygen consumption. Single values of 20 patients. I, Awake; II, III, 5 and 30 minutes after intubation. No significant difference between groups.

were also above the level indicative of a resting state in the majority of patients in both groups (Figs 2 and 3).

Results for haemodynamic variables are presented in

Table 2 and in Figs 1, 4 and 5, and for myocardial variables in Table 3 and Figs 2, 3 and 6. Systolic, diastolic and mean arterial pressures decreased after induction of anaesthesia in both groups with no significant difference between propofol and etomidate. Systolic arterial pressure did not decrease below 100 mmHg in any patient. Systemic vascular resistance was significantly lower in the propofol group. Laryngoscopy and tracheal intubation resulted in a marked increase in systolic and mean arterial pressures in nine patients of the etomidate group and in one patient of the propofol group, accompanied by a (nonsignificant) increase in systemic vascular resistance in both groups. Systolic, diastolic and mean arterial pressures remained significantly decreased to induction values 5 minutes after tracheal intubation in the propofol group and also decreased to induction levels (except for diastolic pressure) in the etomidate group, without significant differences between the two groups. Systemic vascular resistance remained unchanged throughout the subsequent observation period.

Systolic, diastolic and mean arterial pressures were still decreased at induction levels 30 minutes after tracheal intubation without surgical stimulation, with no significant difference from measurements 5 minutes after intubation nor between groups. Mean arterial pressure at this time

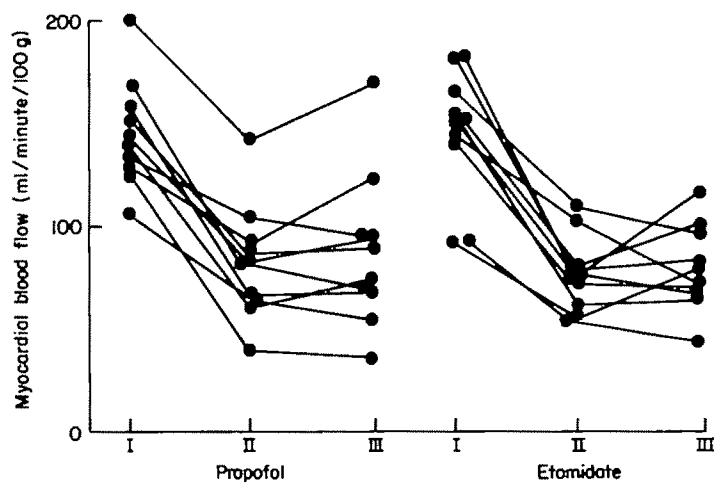


Fig. 3. Changes in myocardial blood flow. Single values of 20 patients. For legend, see Fig. 2. No significant difference between groups.

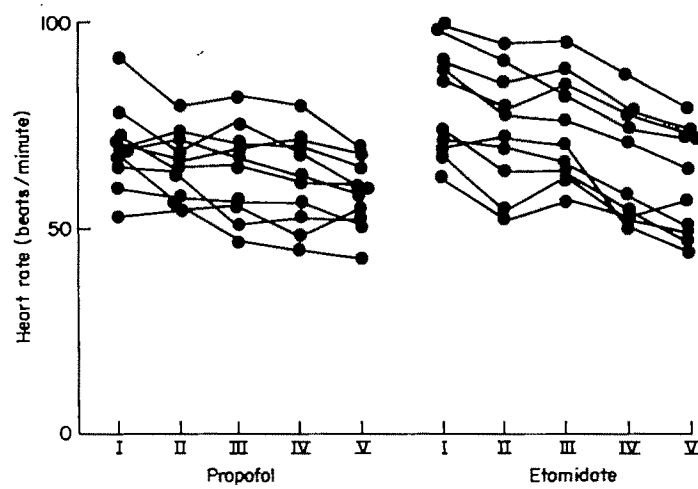


Fig. 4. Changes in heart rate. Single values of 20 patients. For legend, see Fig. 1. Both anaesthetics reduced heart rate significantly to the same extent, with a maximum at 30 minutes after intubation.

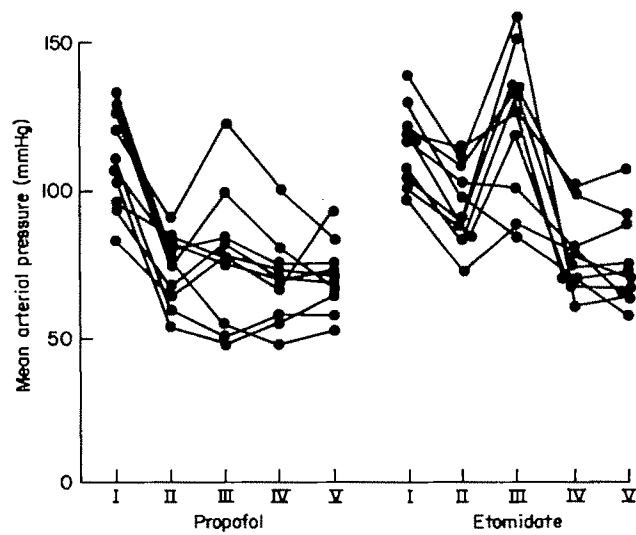


Fig. 5. Effects on mean arterial pressure. Single values of 20 patients. For legend, see Fig. 1. Significant difference between groups at 30 minutes after intubation.

was reduced by 35% from control in both groups. Heart rate remained unchanged after induction with propofol but decreased significantly and progressively with etomidate; this effect was most pronounced 30 minutes after tracheal

intubation (25% from baseline). Heart rate also decreased significantly with propofol to the same level 5 and 30 minutes after tracheal intubation (17% from baseline). Cardiac index was reduced significantly and progress-

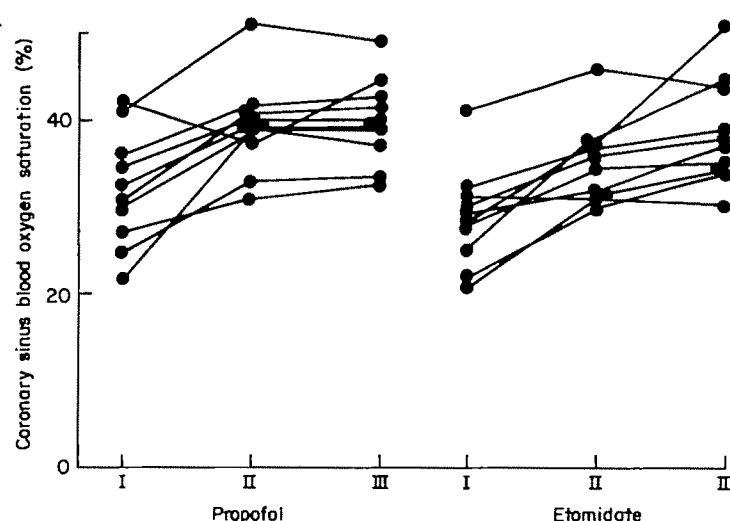


Fig. 6. Effects on coronary sinus blood oxygen saturation. Single values of 20 patients. For legend, see Fig. 2. Significant difference between groups at 5 minutes after intubation.

ively with both anaesthetics; it reached a maximum of 34% below control with propofol and of 37% with etomidate 30 minutes after intubation, with no statistically significant differences between the two anaesthetics. Stroke volume was also reduced in both groups to a similar degree.

Myocardial oxygen consumption and coronary blood flow were decreased significantly in both groups 5 minutes after intubation and remained so 30 minutes later, with no statistically significant difference between propofol and etomidate (Table 3 and Figs 2 and 3). Coronary vascular resistance remained essentially unchanged in both groups throughout the observation period. Coronary sinus blood oxygen saturation increased significantly in both groups; this effect was more pronounced 5 minutes after tracheal intubation in the propofol group (Fig. 6). Myocardial lactate production was not observed in any patient 5 or 30 minutes after tracheal intubation. No electrocardiographic evidence of myocardial ischaemia could be demonstrated at any time in the patients of either group.

Haemoglobin concentration, P_{aO_2} , P_{aCO_2} , pH, base excess, standard bicarbonate and electrolyte concentrations remained within the normal ranges throughout the observation period.

Discussion

Cardiovascular dynamics

Dose requirements for propofol in this investigation were based on preceding dose-finding studies in which we observed an increased sensitivity of geriatric patients to the cardiovascular effects of the drug and subsequently reduced dosage. Etomidate was administered according to the infusion model used previously.⁶

Both drugs produced significant cardiovascular depression, with a mean maximum decrease in mean arterial pressure of 35% and a mean maximum reduction in cardiac index of 35% (propofol) and 37% (etomidate), together with a mean maximum decrease in stroke volume index of about 20% in both groups. Heart rate also decreased with a mean maximum of 17% for propofol and of 25% for etomidate. The decrease in arterial pressures was due to a

reduction in cardiac output and systemic vascular resistance in the propofol group, but to a reduction in cardiac output in the etomidate group.

A decrease in arterial pressure is a uniform reaction of the cardiovascular system to induction of anaesthesia with propofol in healthy subjects and in patients with cardiovascular disease; the extent varies and reported changes range from 15–55%.^{2–4,7–10} Hypotension is caused by a reduction in cardiac output but vasodilatation may also play a role, as suggested by a decrease in systemic vascular resistance in several studies. The magnitude of blood pressure reduction by propofol is related to a variety of factors that include dosage, premedication, administration of opioids and benzodiazepines or nitrous oxide, surgical stimulation, hypovolaemia, heart disease, sympathetic tone and age. The same factors apply to etomidate, which produces minimal cardiovascular effects in healthy subjects¹ although it has greater cardiovascular depressant effects in ASA grade 3 patients and in patients with valvular or ischaemic heart disease, in particular when supplemented by nitrous oxide, benzodiazepines or fentanyl.^{10–12,13} Thus, the exaggerated blood pressure response to both drugs in our patients can be attributed mainly to old age, when cardiovascular adaptation is diminished and blood volume reduced, but also to pre-injection of fentanyl 0.1 mg and to an increase in sympathetic tone, since the majority of patients were hypertensive and had high arterial blood pressures and cardiac output on induction of anaesthesia. These patients are known to be particularly susceptible to the effects of most intravenous anaesthetics and respond with a more precipitous decline in arterial pressure due to sudden reduction in sympathetic activity. This effect is highly undesirable in patients with coronary artery or cerebrovascular disease, since it may result in myocardial or cerebral ischaemia. On the other hand, these patients also often demonstrate marked cardiovascular responses to noxious stimuli during anaesthesia, which may compromise myocardial oxygen balance in patients with coronary artery disease due to an increase in myocardial oxygen demand. Haemodynamic changes in the present study were minimal after tracheal intubation in the propofol group; only one patient developed an increase in systolic blood pressure above 160 mmHg, while nine patients in the etomidate

group demonstrated severe (though short-lasting) increases in systolic and mean arterial pressures.

The reported effects of propofol on heart rate are not uniform and are described as no or minimal change,^{7,14} an increase^{2,4} or even a decrease.^{3,8} The reason for these differing results is unclear. Etomidate, on the other hand, usually has less effect on heart rate than any other intravenous anaesthetic.¹ However, in the present study both agents produced a significant reduction in heart rate which was most pronounced 30 minutes after tracheal intubation, with a decline to less than 60 beats/minute in five patients of each group (of whom three developed heart rates of less than 50 beats/minute in the etomidate group and one in the propofol group). The exact mechanism of the decrease in heart rate with propofol and etomidate in our patients is unknown but it appears to be related to old age, since it is well substantiated that the heart rate response to various stressful stimuli such as hypotension, hypoxia, hypercapnia or exercise, decreases with age. Reduced carotid sinus baroreceptor and sympathetic nervous system activity as well as a decreased end organ response might be involved in the effects of anaesthetics on heart rate in old age.

The significant and progressive reduction in cardiac output with prolonged administration of propofol in our patients is probably due mainly to a negative inotropic effect and to bradycardia; however, reduction in preload might also be involved. Again, old age appears to contribute to the pronounced myocardial depressant effect of both anaesthetics. These findings are essentially in accordance with those of other workers, who also found a significant reduction in cardiac output with propofol in healthy subjects and in patients with heart disease.^{3,4,7,9,10} Etomidate in normal subjects essentially does not affect cardiac output¹ but it does so in patients with heart disease.¹¹⁻¹³ In this study it produced a significant and progressive decline in cardiac output with prolonged administration, of the same magnitude as with propofol. Again, this effect can be attributed mainly to a negative inotropic action (as indicated by a significant decrease in stroke volume) and bradycardia; both effects are enhanced by changes in cardiovascular function with age. Cardiac index was reduced to or beneath the normal lower resting level of 2.2 litres/minute/sq m in three patients of each group but early signs of myocardial failure (i.e. an increase in pulmonary artery wedge pressure) could not be detected. Further studies are required to clarify the contribution of a possible reduction in whole body oxygen demand by propofol and etomidate to the decline in cardiac output.

Myocardial blood flow and oxygen consumption

Propofol and etomidate produced a significant decrease in myocardial oxygen consumption and myocardial blood flow in this study, due to a reduction in heart rate, arterial blood pressure and, presumably, in myocardial contractility, i.e. the major determinants of myocardial oxygen consumption. Coronary sinus oxygen saturation increased and arterial-coronary sinus blood oxygen content difference decreased whereas coronary vascular resistance remained unchanged in both groups. These findings indicate some kind of coronary perfusion in excess of demand, due most probably to a coronary vasodilating effect of both drugs. Coronary perfusion pressure and cardiac output were reduced but coronary perfusion appeared to be

adequate, since no signs of myocardial ischaemia (i.e. myocardial lactate production, increases in pulmonary wedge pressure, electrocardiographic changes) could be detected. The decrease of myocardial blood flow in our patients was obviously caused by the reduction in myocardial oxygen demand, which indicates that the coupling of myocardial metabolism and myocardial blood flow was largely maintained with propofol and etomidate. Similar results were obtained for propofol by Stephen and co-workers⁴ in patients with severe coronary artery disease. They found a 26% and 31% decrease in myocardial blood flow and myocardial oxygen consumption; in our study both effects were more pronounced but this is simply due to the higher baseline levels in our patients, since those with high arterial blood pressures or cardiac output in the awake state also demonstrated high levels of myocardial oxygen consumption and coronary blood flow. These findings indicate a hyperdynamic state of the circulation most probably due to pre-operative excitement, while the patients in Stephen's investigation were heavily premedicated and also received beta-adrenoceptor antagonists and/or calcium-channel blocking drugs. They thus showed lower resting levels of arterial blood pressure and cardiac output and consequently of myocardial oxygen consumption and coronary blood flow.

In conclusion, our data demonstrate that propofol and etomidate impair cardiovascular performance to the same extent in old patients without manifestations of heart disease. Propofol offers protection from the cardiovascular stimulating effects of tracheal intubation but etomidate does not prevent these reactions. In this regard propofol is preferable to etomidate. Both drugs, however, should be used with caution in old patients with severe coronary or cerebral arteriosclerosis, since the pronounced reduction in perfusion pressure might impair adequate blood supply to these organs.

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References

1. SONNTAG H. Actions of anesthetics on the coronary circulation in normal subjects and patients with ischaemic heart disease. In: PRYS-ROBERTS C, ed. *Hypertension, ischaemic heart disease, and anaesthesia*. International Anesthesiology Clinics Vol. 18, No. 4. Boston: Little Brown and Company, 1980: 111-35.
2. AL-KHUDHAIRI D, GORDON G, MORGAN M, WHITWAM JG. Acute cardiovascular changes following disopropofol. Effects in heavily sedated patients with coronary artery disease. *Anaesthesia* 1982; 37: 1007-10.
3. PATRICK MR, BLAIR IJ, FENECK RO, SEBEL PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 23-7.
4. STEPHEN H, SONNTAG H, SCHENK HD, KETTLER D, KHAM-BATTA HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; 48: 969-75.
5. TAUCHERT M, KOCHSIEK K, BEISS HW. Measurements of coronary blood flow in man by the argon method. In: MASERI

- A, ed. *Myocardial blood flow in man*. Turin: Minerva Medica, 1970: 859-65.
6. SCHWILDEN H, STOECKEL H, SCHÜTTLER J, LAUVEN P. Comparison of various empirical dosage suggestions for etomidate infusions on the basis of pharmacokinetic data. *Anästhesie, Intensivtherapie, Notfallmedizin* 1981; **26**: 176-9.
7. PRYS-ROBERTS C, DAVIES JR, CALVERLEY RK, GOODMAN NW. Haemodynamic effects of infusions of diisopropyl phenol (ICI 35 868) during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1983; **55**: 105-11.
8. AUN C, MAJOR E. The cardiorespiratory effects of ICI 35 868 in patients with valvular heart disease. *Anaesthesia* 1984; **39**: 1096-100.
9. COATES DP, PRYS-ROBERTS C, SPELINA RK, MONK CR, NORLEY I. Propofol ('Diprivan') by intravenous infusion with nitrous oxide: dose requirements and haemodynamic effects. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 76-9.
10. ULSAMER B, DOENICKE A, LASCHAT M. Propofol in comparison to etomidate for the induction of anaesthesia. *Anaesthesist* 1986; **35**: 535-42.
11. MURDAY HK, HACK G, SCHÜTTLER J, HEINEMANN, T. Anaesthetic consideration in patients undergoing aorto-coronary bypass graft surgery. Comparison of the haemodynamic influence of two recent total intravenous anaesthetic techniques. *Anästhesie, Intensivtherapie, Notfallmedizin* 1985; **20**: 170-85.
12. MURDAY HK, HACK G, HERMANN E, RUDOLPH A. Haemodynamic effects of a combination of etomidate, flunitrazepam or midazolam with fentanyl for induction of anaesthesia in patients with valvular lesions of the heart. *Anästhesie, Intensivtherapie, Notfallmedizin* 1985; **20**: 175-85.
13. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA, STEPHENSON DK. Dose requirements of ICI 35 868 (propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1168-71.
14. HEMPELMANN G, OSTER W, PEIPENBROCK S, KARLICEK G. Haemodynamic effects of etomidate—a new hypnotic—in patients with myocardial insufficiency. In: DOENICKE A, ed. *Etomidate*. New York: Springer, 1977: 72-80.

Effects of thiopentone, etomidate and propofol on the haemodynamic response to tracheal intubation

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Summary

The haemodynamic response to tracheal intubation was compared in 303 patients in whom anaesthesia was induced with either thiopentone 4 mg/kg, etomidate 0.3 mg/kg or propofol 2.5 mg/kg, with and without fentanyl 2 µg/kg. There was after propofol alone a significant decrease in arterial blood pressure, which did not increase above control values after intubation. Significant increases in arterial pressure followed intubation in patients induced with thiopentone or etomidate alone. Increases in heart rate occurred with all agents after laryngoscopy. The use of fentanyl resulted in arterial pressures lower than those after the induction agent alone, and in an attenuation, but not abolition of the responses to laryngoscopy and intubation.

Key words

Anaesthetics, intravenous; propofol, etomidate, thiopentone. Intubation, tracheal.

The haemodynamic consequences of laryngoscopy and tracheal intubation have been reported for many years^{1–4} and may be severe enough to have serious myocardial^{5–8} and cerebral effects.^{5–9} Several methods have been described to protect against this response.^{10–19} It was noted recently that these changes are attenuated, although not abolished after induction of anaesthesia with propofol.^{20–23}

The present study investigated the effects of three induction agents, thiopentone, etomidate and propofol, with and without fentanyl, on the haemodynamic response to tracheal intubation.

Methods

Studies were carried out on 303 patients between 16 and 60 years of age, ASA grade 1 or 2, who were to undergo surgery that required tracheal intubation. Hypertensive patients or those with known allergy to any of the drugs used were not studied. The protocol also allowed exclusion of the results of any patient who proved difficult to intubate or who coughed during tracheal intubation; there were 12 such patients in the study.

The patients were randomly allocated into six groups to receive the following induction agents: thiopentone 4 mg/kg with and without fentanyl 2 µg/kg; etomidate 0.3 mg/kg with and without fentanyl 2 µg/kg; and propofol 2.5 mg/kg with and without fentanyl 2 µg/kg. All patients received

intramuscular premedication with atropine 0.6 mg and papaveretum 1–1.5 hours before operation. The dose of papaveretum varied according to the patients' weight: < 50 kg, 10 mg; 50–70 kg, 15 mg; and > 70 kg, 20 mg.

Procedure

A conventional four-lead ECG was attached on arrival in the anaesthetic room and lead 2 displayed continuously. A strip recorder was used to identify any dysrhythmias. An automatic blood pressure cuff (Dinamap) was attached to one arm and an indwelling cannula inserted into a vein in the other arm for drug administration. Measurements of arterial blood pressure were made 10 minutes, 5 minutes and immediately prior to induction.

Fentanyl 2 µg/kg (or an appropriate volume of saline) was then injected over 30 seconds. The induction agent was also injected over 30 seconds, one minute after the start of the fentanyl injection and immediately after measurements had been made. The patient then breathed 70% nitrous oxide in oxygen via a Magill system; ventilation was assisted gently if necessary. Suxamethonium 1.5 mg/kg was injected during 15 seconds immediately after the next measurements, one minute after the start of induction, and ventilation controlled. The trachea was intubated with a cuffed tube 2 minutes after the start of the suxamethonium injection and the lungs ventilated with the same mixture. Measurements were taken immediately prior to laryngo-

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Table 1. Mean (SD) ages and weights and distribution of males and females between the groups.

Induction	Age, years	Weight, kg	Sex, M/F
Thiopentone (n = 51)	34.0 (7.35)	60.6 (9.25)	5/46
Thiopentone-fentanyl (n = 50)	34.0 (7.87)	64.9 (13.02)	4/46
Etomidate (n = 51)	36.0 (9.7)	65.2 (11.45)	11/40
Etomidate-fentanyl (n = 50)	35.8 (7.28)	66.7 (13.12)	8/42
Propofol (n = 51)	33.5 (7.02)	64.4 (11.01)	11/41
Propofol-fentanyl (n = 50)	35.7 (9.7)	65.6 (14.88)	10/40

scopy and intubation and then at one-minute intervals until there was evidence of return of neuromuscular function.

Statistical tests were analysis of variance, the paired and unpaired *t*-test and Chi-squared tests.

Results

Patient data are given in Table 1. There was no significant difference between the groups with regard to weight, age or the distribution of males and females. The preponderance of the latter was due to the inclusion of gynaecological patients.

Arterial blood pressure

There were no significant differences in arterial pressure 10 or 5 minutes before the induction sequence and hence only the results immediately before the induction are presented. There were no differences in the control readings between the six groups.

The changes in arterial systolic and diastolic blood pressures after the induction agents alone are shown in Fig. 1. There were no significant changes after thiopentone and

etomidate up to the point of tracheal intubation. In contrast, arterial pressure decreased significantly after propofol and just prior to intubation was highly significantly lower than control values, and compared with thiopentone and etomidate ($p < 0.01$ in each case).

There was a significant increase ($p < 0.001$) in arterial pressure after intubation in all three groups compared to pre-intubation levels but in the case of propofol the arterial pressure did not increase above the pre-induction values. There was a highly significant ($p < 0.001$) increase above control levels with thiopentone and etomidate. Thereafter, arterial pressure decreased slightly over the next 2 minutes in all three groups. Considerable individual variation was associated with all three drugs. The lowest systolic pressure recorded was 80 mmHg one minute after propofol. The highest systolic pressures recorded one minute after intubation were 183 mmHg after thiopentone, 231 mmHg after etomidate and 175 mmHg after propofol. The highest figures for diastolic pressure were 146, 156 and 121 mmHg, respectively.

The influence of fentanyl on the pressor response to intubation is shown in Fig. 2-4. Arterial pressure after thiopentone and fentanyl (Fig. 2) was significantly lower ($p < 0.001$) just prior to intubation than after thiopentone alone. The arterial pressure after tracheal intubation in the thiopentone-fentanyl group increased by a similar amount as in those given thiopentone alone but it did not exceed pre-induction values. Similar patterns were seen after etomidate-fentanyl (Fig. 3) and propofol-fentanyl (Fig. 4). Arterial pressure in both these groups was significantly lower just prior to intubation when fentanyl was used. The

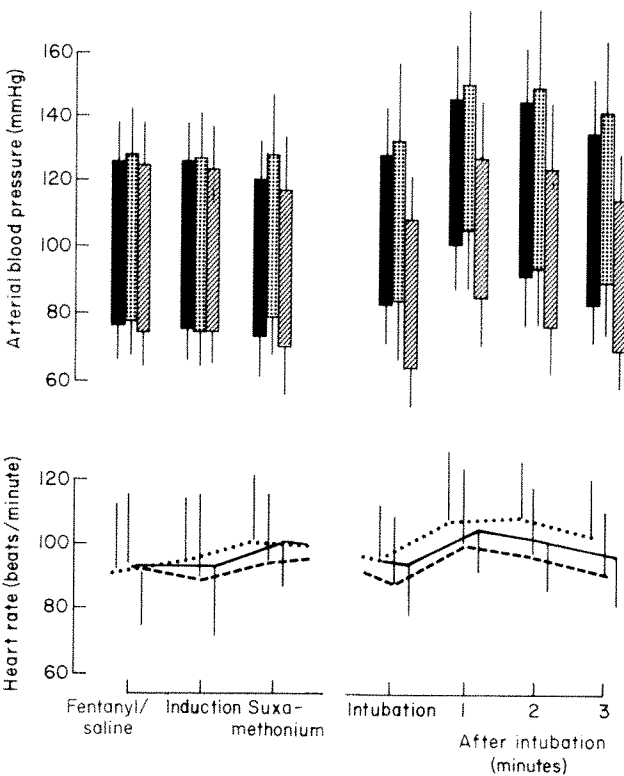


Fig. 1. Changes in arterial pressure and heart rate after induction of anaesthesia with thiopentone 4 mg/kg, etomidate 0.3 mg/kg and propofol 2.5 mg/kg. ■, Thiopentone; □, etomidate; ▨, propofol. For statistical significance, see text.

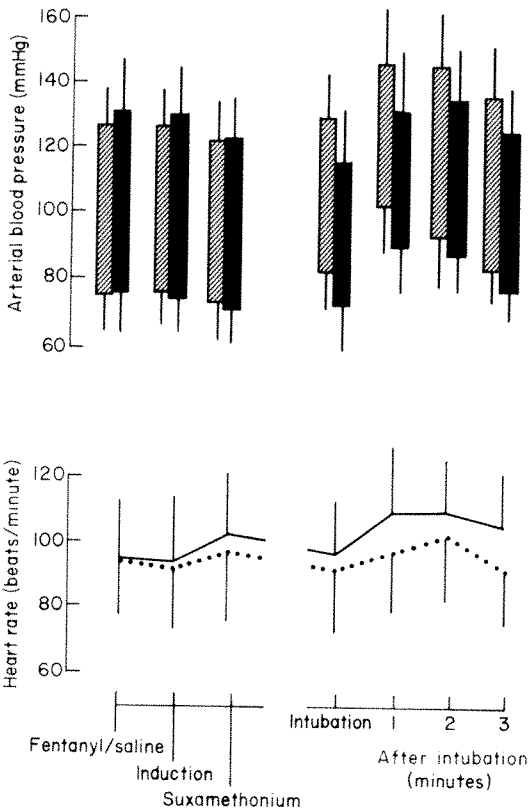


Fig. 2. Effect of fentanyl 2 µg/kg on the haemodynamic response to tracheal intubation after induction of anaesthesia with thiopentone 4 mg/kg. ▨, Thiopentone; ▨, thiopentone-fentanyl. For statistical significance, see text.

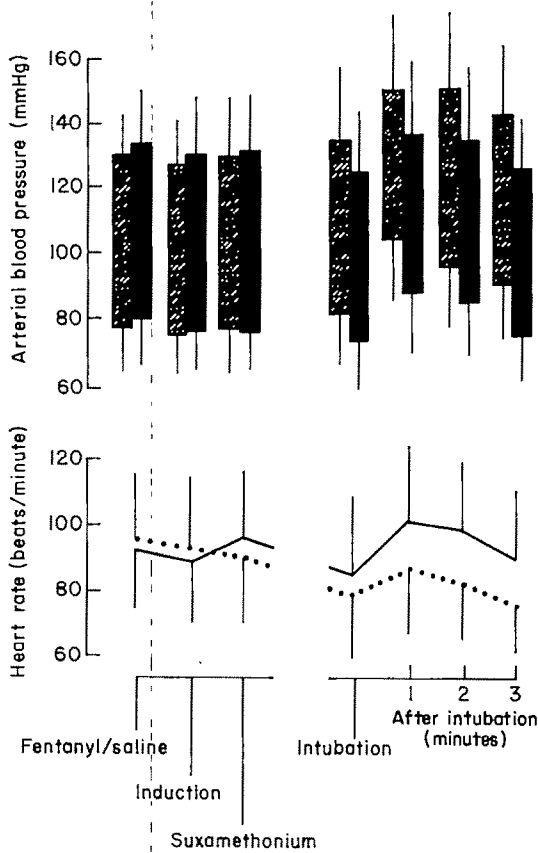


Fig. 3. Effect of fentanyl 2 µg/kg on the haemodynamic response to tracheal intubation after induction of anaesthesia with etomidate 0.3 mg/kg. ■, —, Etomidate; ■, ····, etomidate-fentanyl. For statistical significance, see text.

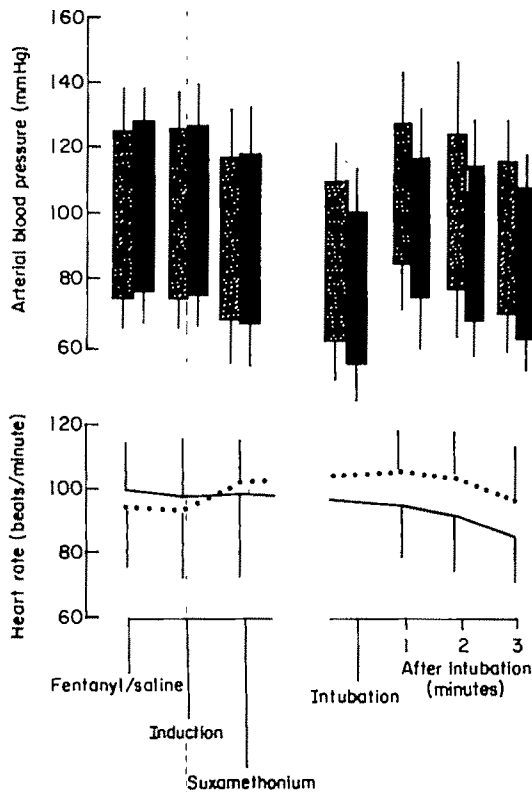


Fig. 4. Effect of fentanyl 2 µg/kg on the haemodynamic response to tracheal intubation after induction of anaesthesia with propofol 2.5 mg/kg. ■, ····, Propofol; ■, —, propofol-fentanyl. For statistical significance, see text.

Table 2. Type and incidence of dysrhythmias.

Induction	Number with dysrhythmias	Type
Thiopentone (n = 51)	2	1 bradycardia, 1 supra-ventricular tachycardia
Thiopentone-fentanyl (n = 50)	7	1 sinus bradycardia with ventricular ectopics, 1 sinus bradycardia, 3 nodal rhythm, 1 bi-gemini, 1 supra-ventricular tachycardia
Etomidate (n = 51)	7	1 bradycardia progressing to bigemini, 1 nodal bradycardia progressing to bigemini, 1 atrial and ventricular ectopics, 1 supra-ventricular tachycardia, 1 bradycardia, 1 bigemini, 1 ventricular ectopics
Etomidate-fentanyl (n = 50)	5	5 bradycardias
Propofol (n = 51)	3	2 ventricular ectopics, 1 supra-ventricular tachycardia
Propofol-fentanyl (n = 50)	3	2 nodal rhythm, 1 bigemini

increases in arterial pressure after intubation were again similar to those when the induction agent was given by itself but inclusion of fentanyl prevented an increase of the arterial pressure above control levels.

Heart rate

The changes in heart rate are also shown in Figs 1–4. There were no significant differences in heart rate between the six groups just prior to induction. Thiopentone and propofol were accompanied by an increase in heart rate but in both groups this returned to pre-induction levels just prior to intubation. The mean heart rate in the etomidate group was 7 beats/minute slower ($p < 0.05$) than control just before intubation; significant increases in heart rate followed intubation in each group ($p < 0.01$ in each case) and the greatest increase was an average of 14 beats/minute in those given etomidate.

Prior administration of fentanyl abolished the increase in heart rate associated with induction of anaesthesia. There was a reduction in heart rate just before intubation in each group that received fentanyl, which was highly significant ($p < 0.001$) in the case of etomidate-fentanyl and significant at the 1% level in the case of propofol-fentanyl. The change did not reach statistical significance in the case of thiopentone-fentanyl. The tachycardia after intubation was markedly attenuated, although not entirely prevented and only in the case of thiopentone-fentanyl did heart rate exceed pre-induction levels.

Dysrhythmias

Dysrhythmias were seen in 27 patients (9%) and their type and distribution among the groups are shown in Table 2. The highest incidence occurred in those who were induced with thiopentone-fentanyl and etomidate alone but there was no statistical difference between the groups. The commonest disturbances of rhythm were associated with bradycardia (< 50 beats/minutes). They were all of a transient

nature, occurred mainly at the time of intubation and no treatment was thought necessary. Some patients had more than one type of dysrhythmia.

Discussion

The commonest cardiovascular response to intubation is an increase in heart rate and arterial blood pressure due to an increase in sympathetic activity,¹ although bradycardias associated with increased parasympathetic activity, are also common.²⁴ Myocardial oxygenation in patients with coronary insufficiency may be severely compromised under these circumstances and ischaemic changes and actual infarction have been reported.^{6,7,8} Hypertension and tachycardia predispose to dysrhythmias,²⁴ while the ejection fraction decreases during laryngoscopy and intubation.²⁵ Cases of frank left ventricular failure have been described.⁵ Cerebral haemorrhage may also occur⁵ and convulsions may be precipitated in mothers with pre-eclampsia.⁹ Hypertensive patients, even if they receive therapy, are par-tachycardias and dysrhythmias.^{13,15}

Several methods have been used in an attempt to ablate this response. Surface anaesthesia of the larynx and pharynx with lignocaine spray proved unsuccessful because of the need to perform laryngoscopy with resultant stretching and pressure on the tissues of the larynx and pharynx.^{13,14} It is interesting that blind nasal intubation, without laryngoscopy, did not result in any cardiovascular sequelae.⁴ Intravenous lignocaine in a dose of 1.5 mg/kg effectively ablates the hypertensive response and prevents tachycardias and dysrhythmias.^{13,15}

Deep anaesthesia reduces the cardiovascular effects of laryngoscopy and intubation,¹ although volatile agents appear to control the changes in arterial pressure more effectively than the changes in heart rate.¹⁰ However, deep anaesthesia does not allow rapid sequence intubation and may result in prolonged recovery after short procedures. The associated hypotension may also be undesirable, particularly in patients with coronary insufficiency.

Fentanyl 5 µg/kg at induction of anaesthesia effectively prevents the haemodynamic effects of tracheal intubation, while smaller doses attenuate it.^{10-12,16,17} Alfentanil 30 µg/kg¹⁷ and sufentanil 0.5-1.0 µg/kg²⁶ are also effective. However, the respiratory depression associated with these drugs may be a problem in short procedures, although less so with alfentanil.

Beta-adrenoceptor blockade has been advocated as a method to protect against the effects of laryngoscopy, particularly in patients with pre-existing hypertension.^{4,18} Variable effectiveness has been reported and the long duration of action may be associated with hypotension and bradycardia during the remainder of the procedure. Vasodilators may also result in profound hypotension once the stimulus of laryngoscopy is removed. Sodium nitroprusside, which has an evanescent action, has been recommended¹⁹ but requires intensive monitoring and may itself cause a tachycardia.

The present study set out to compare three commonly used induction agents with and without a relatively small dose of fentanyl. Laryngoscopy and intubation after thiopentone and etomidate alone was accompanied by significant increases in heart rate and arterial pressure above control levels. The increases in pressure, particularly with etomidate, were occasionally alarming, for example 231/156

mmHg. In contrast, the changes after intubation in the propofol group did not exceed control values but the arterial pressure just prior to laryngoscopy in these patients was significantly lower than the pre-induction arterial pressure. Similar changes have been found by others.²¹⁻²³ Addition of a small dose of fentanyl to each induction agent resulted in attenuation, but not abolition of the response.

The incidence of dysrhythmias during intubation has been variously reported from 0-90%.²⁴ The 9% incidence in the present study is relatively low, probably because of the use of ASA grade 1 or 2 patients without hypertension, and the avoidance of volatile agents. The commonest dysrhythmia was bradycardia despite the use of atropine in the premedication.

This study shows that a single induction dose of propofol attenuates, but does not prevent the haemodynamic response to laryngoscopy and intubation. Induction, however, is accompanied by a significant decrease in arterial blood pressure. Induction with propofol alone is a suitable method in fit patients where it is deemed necessary to attenuate the response and where administration of a narcotic is undesirable. In patients who are at risk, it is up to the anaesthetist to decide whether the benefits of attenuated effects of intubation outweigh the possible risks of the decrease in arterial pressure associated with induction. The use of a small dose of fentanyl with thiopentone or etomidate may also be an acceptable method but induction with thiopentone or etomidate alone is not acceptable when the haemodynamic responses to tracheal intubation need to be obtunded.

Acknowledgments

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References

- KING BD, HARRIS LC Jr, GREIFENSTEIN FE, ELDER JD, DRIPPS RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. *Anesthesiology* 1951; **12**: 556-66.
- WYCOFF CC. Endotracheal intubation: effects on blood pressure and pulse rate. *Anesthesiology* 1960; **21**: 153-8.
- FORBES AM, DALLY FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42**: 618-24.
- PRYS-ROBERTS C, GREENE LT, MELOCHE R, FOEX P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1971; **43**: 531-46.
- FOX EJ, SKLAR GS, HILL CF, VILLANUEVA R, KING BD. Complications related to the pressor responses to endotracheal intubation. *Anesthesiology* 1977; **47**: 524-5.
- MOFFITT EA, SETHNA DH. The coronary circulation and myocardial oxygenation in coronary artery disease: effects of anaesthesia. *Anesthesia and Analgesia* 1986; **65**: 395-410.
- MOFFITT EA, SETHNA DH, BUSSELL JA, RAYMOND MJ, MATLOFF J, GRAY RJ. Effects of intubation on coronary blood flow and myocardial oxygenation. *Canadian Anaesthetists' Society Journal* 1985; **32**: 105-11.
- BUFFINGTON CW. Hemodynamic determinants of ischemic myocardial dysfunction in the presence of coronary stenosis in dogs. *Anesthesiology* 1985; **63**: 651-62.
- MATERNAL AND PERINATAL MORTALITY COMMITTEE, NEW SOUTH WALES. Caesarean section in New South Wales 1966-1967: a mortality and morbidity study. *Medical Journal of Australia* 1969; **1**: 319-20.
- endotracheal intubation during four anaesthetic techniques. *Acta Anaesthesiologica Scandinavica* 1984; **28**: 563-6.

11. KAUTTO VM. Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 217-21.
12. DAHLGREN N, MESSETER K. Treatment of stress response to laryngoscopy and intubation with fentanyl. *Anaesthesia* 1981; **36**: 1022-6.
13. STOELTING RK. Circulatory changes during direct laryngoscopy and tracheal intubation. Influence of duration of laryngoscopy with or without prior lidocaine. *Anesthesiology* 1977; **47**: 381-4.
14. DENLINGER JK, ELLISON N, OMINSKY AJ. Effects of intratracheal lidocaine on circulatory responses to tracheal intubation. *Anesthesiology* 1974; **41**: 409-12.
15. ABOU-MADI MN, KESZLER H, YACOB JM. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. *Canadian Anaesthetists' Society Journal* 1977; **24**: 12-19.
16. KAY B, HEALY TEJ, BOLDER PM. Blocking the circulatory responses to tracheal intubation. A comparison of fentanyl and nalbuphine. *Anaesthesia* 1985; **40**: 960-3.
17. BLACK TE, KAY B, HEALY TEJ. Reducing the haemodynamic responses to laryngoscopy and intubation. A comparison of alfentanil with fentanyl. *Anaesthesia* 1984; **39**: 883-7.
18. PRYS-ROBERTS C, FOEX P, BIRO GP, ROBERTS JG. Studies of anaesthesia in relation to hypertension. V. Adrenergic β receptor blockade. *British Journal of Anaesthesia* 1973; **45**: 671-81.
19. STOELTING RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. *Anesthesia and Analgesia* 1979; **58**: 116-9.
20. PATRICK MR, BLAIR IJ, FENECK RO, SEBEL PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 23-7.
21. COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE M, NORLEY I, SPELINA KR. Haemodynamic responses to induction and endotracheal intubation with propofol/nitrous oxide anaesthesia. *European Journal of Anaesthesia* 1986; **3**: 65-6.
22. COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE M. Hemodynamic effects of the infusions of the emulsion formulation of propofol during nitrous oxide anaesthesia in humans. *Anesthesia and Analgesia* 1987; **66**: 64-70.
23. MONK CR, COATES DP, PRYS-ROBERTS C, TURTLE MJ, SPELINA K. Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia. Studies in association with peripheral arterial surgery. *British Journal of Anaesthesia* 1987; **59**: 954-60.
24. KATZL RL, BIGGER JT. Cardiac arrhythmias during anaesthesia and operation. *Anesthesiology* 1970; **33**: 193-213.
25. BARASH PG, KIPRIVA CD, GILES R, TARABADKAR S, BERGER H, ZARET B. Global ventricular function and intubation, radionuclear profiles. *Anesthesiology* 1980; **53**: S109.
26. KAY B, NOLAN D, MAYALL R, HEALY TEJ. The effect of sufentanil on the cardiovascular responses to tracheal intubation. *Anaesthesia* 1987; **42**: 382-6.

Effect of propofol on cerebrospinal fluid pressure and cerebral perfusion pressure in patients undergoing craniotomy

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Summary

The effects of propofol on cerebrospinal fluid pressure, mean arterial pressure, cerebral perfusion pressure and heart rate were studied during induction, tracheal intubation and skin incision in 23 patients scheduled for elective craniotomy. Premedication consisted of midazolam 0.1 mg/kg intramuscularly and metoprolol 1 mg/kg orally. Measurements were made or derived at time zero and 0.5, 1, 1.5, 2 and 3 minutes after an induction dose of propofol 1.5 mg/kg. A continuous infusion of propofol was started at time zero at a rate of 100 mg/kg/minute. Fentanyl 2 µg/kg was added before tracheal intubation, application of the pin head holder and skin incision. Cerebrospinal fluid pressure and mean arterial pressure decreased significantly 2 minutes after propofol alone, by 32% and 10% respectively, while a cerebral perfusion pressure above 70 mmHg was maintained. Heart rate did not change. Propofol combined with moderate dose of fentanyl, obtunded the usual cerebrospinal fluid and arterial pressure responses to intubation and other noxious stimuli. Thus propofol seems to be a suitable intravenous anaesthetic agent for induction and maintenance in neuroanaesthesia.

Key words

Anaesthetics, intravenous; propofol.

Measurement techniques; cerebrospinal fluid pressure.

Total intravenous anaesthesia has always received much attention in neuroanaesthesia as a means to avoid the cerebral vasodilating effects of nitrous oxide and the volatile agents.^{1,2} However, it has not been used widely, because of the adverse allergic reactions encountered with preparations that contain Cremophor,^{3,4} the delayed recovery observed with barbiturates and benzodiazepines and the effect of etomidate on cortisol production. Propofol in its new aqueous emulsion formulation possesses many of the properties required for total intravenous anaesthesia, in particular a short recovery time^{5,6} despite the evidence of accumulation in long procedures⁵, but its effects on cerebrospinal fluid (CSF) pressure and cerebral perfusion pressure in patients who undergo elective craniotomy are unknown. This open, non-comparative study was designed to evaluate the effect of propofol on CSF and cerebral perfusion pressure during the crucial period of induction, tracheal intubation and skin incision in patients scheduled for elective craniotomy.

Methods

Twenty-three consecutive, adult ASA grade 3 patients scheduled for elective intracranial surgery were studied after

ethical committee approval and informed consent. Patients were not studied if their intracranial pathology could obstruct the CSF pathway between the lateral ventricles and the lumbar cisterna, or if an intraventricular drain was already in place. For these reasons, changes in CSF pressure were considered to indicate changes in intracranial pressure.⁷ Patients with cardiac, renal or hepatic disease, or in whom a lumbar drain was not essential for management, were also not studied. All patients with an intracranial tumour were receiving steroids and all 23 patients had a Glasgow coma scale score of 15 and no clinical signs of intracranial hypertension.

Anaesthetic and measurement protocol

Premedication consisted of midazolam 0.1 mg/kg intramuscularly and metoprolol 1 mg/kg orally given 1 hour before induction of anaesthesia. Patients were maintained at normothermia and without stimulation during the first 5–8 minutes of the study before tracheal intubation. Normal saline 2ml/kg/hour was infused to maintain hydration. Lumbar CSF pressure, using a 20-gauge malleable spinal needle placed in the lumbar subarachnoid space, mean arterial pressure via a 20-gauge catheter inserted into the

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right femoral artery, heart rate and cerebral perfusion pressure (mean arterial pressure – CSF pressure), were all measured or derived at time zero (baseline) and 0.5, 1, 1.5, 2 and 3 minutes after an induction dose of propofol 1.5 mg/kg injected over 30 seconds. A continuous infusion of propofol 100 µg/kg/minute⁶ was started at the same time as the induction dose with an IVAC Model 531 infusion pump (IVAC Inc., San Diego, California, USA),

Arterial and CSF pressures were measured in the supine position using previously calibrated Model 800 Bentley Trantec strain-gauge transducers referred to the lateral midthoracic line and the external auditory meatus, respectively (Bentley Laboratory Inc., Irvine, California, USA). Mean pressures were determined by electronic integration of the respective transducer signals using a two-channel Model 78342A Hewlett-Packard System (Hewlett-Packard Inc., Paulo Alto, California, USA).

Pancuronium 1 mg/kg and fentanyl 2 µg/kg were injected 2 minutes after the induction dose of propofol and controlled ventilation performed by facemask (FIO₂, 1.0) and then mechanically after tracheal intubation. Paco₂ was maintained at a steady level of 4.5–5.1 kPa as monitored with an Engström Eliza Duo infrared end tidal carbon dioxide analyser (Gambo Engström AG, Bromma, Sweden), and verified by arterial blood gas analysis using an ABL3 Radiometer device (Radiometer CD, Copenhagen, Denmark). Tracheal intubation was performed once full muscle relaxation was confirmed by loss of twitch height and an adequate depth of anaesthesia was present, i.e. 5–8 minutes after the induction dose and the concomitant start of the continuous infusion of propofol. Lignocaine 1.5 mg/kg was injected one minute before intubation. The baseline values for intubation, application of the pin head holder and skin incision were those at one minute before intubation. Fentanyl 2.0 µg/kg was given 5 minutes before application of the pin head holder and skin incision. An intravenous bolus of propofol 20mg was given in cases of inadequate depth of anaesthesia and/or increasing CSF or mean arterial pressures (> 10 mmHg and > 30 mmHg increases, respectively) during intubation, application of the pin head holder or skin incision.

Data analysis

Time zero was the baseline for comparison with values 0.5, 1, 1.5, 2 and 3 minutes later and at one minute before intubation. Values at the latter time were the baseline for comparison with those at intubation, application of the pin head holder and skin incision. Values at intubation were the baseline for comparison with those 1 and 5 minutes later. Student's paired *t*-test with correction for multiple comparisons was used for statistical analysis and *p* < 0.05 was considered to indicate statistical significance. All values are expressed as means, (SEM).

Results

The mean age and weight of the patients were 54 years (SEM 3.6) and 67 kg (SEM 2.4), respectively. Intracranial surgery was for tumour resection (15 patients), aneurysm clipping at Hunt's grades I and II (six patients), trigeminal neuralgia (one patient) and CSF fistula (one patient). The mean duration of the study, from induction to skin incision,

Table 1. Mean (SEM) cerebrospinal fluid pressure (CSFP), arterial pressure (MAP), cerebral perfusion pressure and heart rate before and after an induction dose of propofol 1.5 mg/kg.

	Before induction dose					After induction dose					1 minute before intubation	After intubation		Application of pin head holder†	Skin incision†
												Intubation†	5 minutes		
	0.5 minutes	1 minute	1.5 minutes	2 minutes	7 minutes	1 minute	1.5 minutes	2 minutes	7 minutes						
CSF pressure, mmHg	11.9 (1.4)	9.0 (1.3)*	8.1 (1.2)*	7.5 (1.0)*	8.1 (1.0)*	9.7 (1.5)	11 (1.8)	16.6 (2.7)	9.4 (1.4)	9.0 (1.3)	10.1 (1.1)	9.5 (1.0)			
Mean arterial pressure, mmHg	97 (2.3)	97 (2.8)	92 (2.4)*	87 (2.4)*	87 (3.1)*	85 (2.6)*	84 (2.8)*	89 (3.1)	85 (3.7)	83 (2.8)*	97 (3.1)	94 (3.1)			
Cerebral perfusion pressure, mmHg	85 (2.3)	88 (2.8)	84 (4.4)	79 (2.7)*	79 (3.1)	76 (3.1)*	73 (3.2)*	72 (2.8)	76 (4.1)	74 (4.6)	87 (4.7)	84 (3.2)			
Heart rate, beats/minute	63 (2.2)	65 (3.0)	65 (2.3)	64 (2.5)	64 (2.5)	64 (2.4)	66 (2.5)	72 (2.4)	71 (2.4)	71 (2.9)	69 (2.1)	69 (2.1)			

* *p* < 0.05. † Highest values recorded during intubation, application of the pin head holder and incision. Values before induction dose taken as baseline for comparisons 0.5, 1, 1.5, 2, 3 minutes later and 1 minute before intubation. Values 1 minute before intubation taken as baseline for comparisons at intubation, on application of pin head holder and at skin incision. Values at intubation taken as baseline for comparison 1 and 5 minutes later.

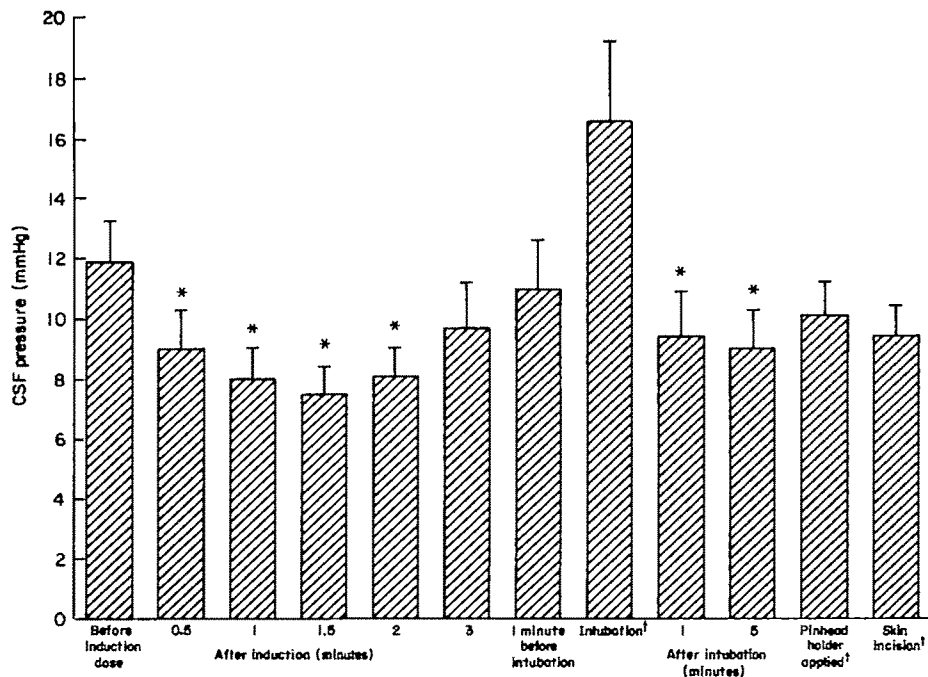


Fig. 1. Mean (SEM) CSF pressure before and after an induction dose of propofol 1.5 mg/kg. * $p < 0.05$, Baselines for comparison as in Table 1. † Maximum values observed.

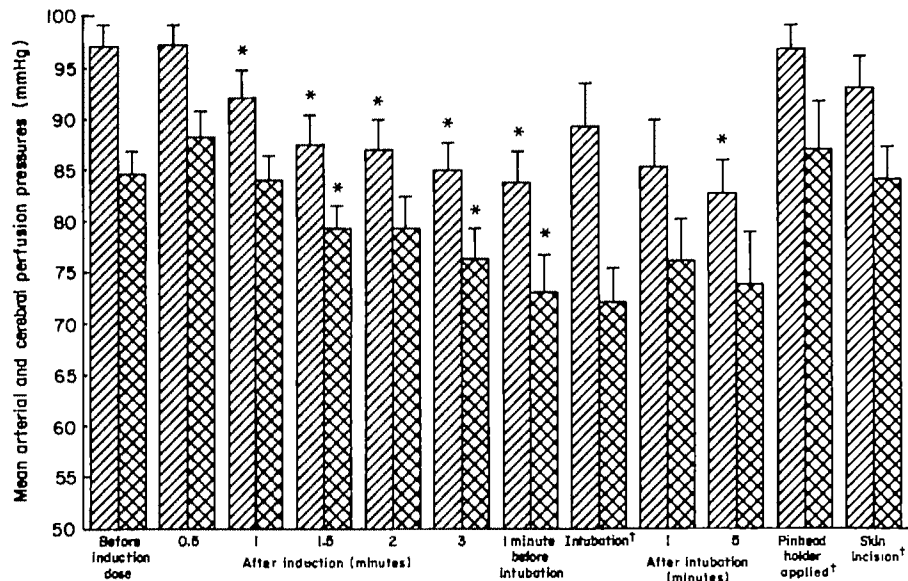


Fig. 2. Mean (SEM) arterial and cerebral perfusion pressures before and after an induction dose of propofol 1.5 mg/kg. ▨, Mean arterial pressure; ▩, cerebral perfusion pressure. * $p < 0.05$, Baselines for comparison as in Table 1. † Maximum values observed.

was 53 minutes (SEM 2.8). Intubation was performed 5.1 minutes (SEM 0.22) after induction.

Mean values of each variable at each time interval are shown in Table 1. Three patients had a baseline CSF pressure above 15 mmHg and one patient had a CSF pressure above 20 mmHg. CSF pressure and mean arterial pressure had decreased significantly 2 minutes after the administration of propofol alone (by 32% and 10%, respectively) but CSF pressure approached baseline values by 3 minutes (Fig. 1). Cerebral perfusion pressure did not decrease after propofol alone up to 2 minutes after the induction dose. There was no significant change in heart

rate at any time. Tracheal intubation, application of the pin head holder and skin incision did not provoke a significant increase in CSF or mean arterial pressure. The lowest mean cerebral perfusion pressure (72 mmHg, SEM 2.7) was seen at intubation when there was a 5.6 mmHg mean increase in CSF pressure (not significant), associated with an almost unchanged mean arterial pressure (Fig. 2).

Thirteen patients (57%) required a bolus of propofol, eight at the time of intubation and five at application of the pin head holder. Anaesthesia and recovery were uneventful in all patients. Their tracheas were extubated in the operating theatre and none reported awareness.

Discussion

Propofol significantly decreased CSF and mean arterial pressures in the present study while it conserved the cerebral perfusion pressure above 70 mmHg. CSF pressure after the initial decrease returned towards baseline values 3 minutes after the induction dose of propofol 1.5 mg/kg, which demonstrates the drug's transient properties and the need to achieve rapidly a plasma concentration plateau,⁸ particularly when it is used for total intravenous anaesthesia in neurosurgical patients.

The maintenance dose of propofol suggested by Spelina et al.⁶ was adequate for patients who received fentanyl, except at the time of intubation, when eight required a supplementary dose of 20 mg. The need for a supplement can be explained by an inadequate propofol plasma concentration at that time in those eight patients.

No change in CSF pressure after a low dose of propofol (1 mg/kg) was reported in patients with head injuries.⁹ Nevertheless, propofol has been shown to increase cerebrovascular resistance,¹⁰ as do barbiturates,¹¹ etomidate,¹² Althesin¹³ and midazolam.¹⁴ With all these agents, a decrease in intracranial pressure accompanies the increase in cerebrovascular resistance and is presumed to result from a concomitant decrease in cerebral blood volume.^{11,12,15} The higher the intracranial pressure, the more important will be the decrease in pressure after an induction dose of one of these agents until the patients have returned to the flat portion of the pressure-volume curve.¹¹ The intracranial pressure decreasing effect of these agents will be only minor starting from that part of the curve.^{9,11,15}

An important assumption in this study is that the lumbar CSF pressure reflects intracranial pressure in patients with and without intracranial hypertension. The patients studied were clinically free of pathology judged likely to obstruct CSF pathways between the intracranial and lumbar CSF spaces. Experimental analysis of volume-pressure relationships at various locations in the neuraxis during inflation of an epidural balloon⁷ revealed that an intracranial-cisterna magna pressure gradient develops when the lateral ventricular pressure is approximately 20 mmHg. If these canine data can be extrapolated to human subjects, only one patient should have had at most a small intracranial-lumbar CSF pressure gradient and the CSF pressure measured during the present study should accurately reflect intracranial pressure.

Propofol has been shown previously to cause a decrease in mean arterial pressure at induction of between 15 and 30% because of various decreases in systemic vascular resistance and cardiac output.^{16,17} The magnitude of this decrease was of concern at the start of this study because maintenance of cerebral perfusion pressure is of utmost importance in patients scheduled for intracranial surgery. However, the maximal decrease in mean pressure was only 10% (14% once fentanyl was added) with the induction dose used in this study. Heart rate did not change significantly at any time. This is probably because all our neurosurgical patients receive a beta-adrenoceptor blocker, when not contraindicated, as part of their pre-operative medication.¹⁸ Furthermore, propofol *per se* induces minimal changes in heart rate.^{16,17}

Propofol associated with fentanyl¹⁹ and 1 mg/kg lignocaine,²⁰ obtunded the usual CSF and mean arterial pressure responses associated with tracheal intubation, ap-

plication of the pin head holder and skin incision. This contrasts with the results found in a recent study when thiopentone or midazolam alone were used for induction and as a pretreatment, 1 and 2.5 minutes respectively before intubation in patients with brain tumours.¹⁵ Thus, the combination of propofol and fentanyl in premedicated patients seems able to block effectively the autonomic sympathetic responses to such noxious stimulation.²¹

In conclusion, propofol decreases intracranial pressure and maintains cerebral perfusion pressure with rapid and complete recovery after administration. It therefore appears to be a suitable short-acting intravenous anaesthetic agent for induction and maintenance of general anaesthesia in neurosurgical patients. The cerebral vasodilating action of inhalational agents can thus be avoided.

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References

1. DRUMMOND JC, TODD MM, TOUTANT SM, SHAPIRO HM. Brain surface protrusion during enflurane, halothane, and isoflurane anaesthesia in cats. *Anesthesiology* 1983; **59**: 288-93.
2. MANOHAR M, PARKS C. Regional distribution of brain and myocardial perfusion in swine while awake and during 1.0 and 1.5 MAC isoflurane anaesthesia produced without or with 50% nitrous oxide. *Cardiovascular Research* 1984; **18**: 344-53.
3. WATKINS J, CLARK A, APPELYARD TN, PADFIELD A. Immune-mediated reaction to Althesin (alphaxalone). *British Journal of Anaesthesia* 1976; **48**: 881-6.
4. BRIGGS LP, CLARKE RSJ, WATKINS J. An adverse reaction to the administration of disopropofol (Diprivan). *Anaesthesia* 1982; **37**: 1099-101.
5. DE GROOD PMRM, RUYS AHC, VAN EGMOND J, BOOL, CRUL JF. Propofol (Diprivan) emulsion for total intravenous anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 65-9.
6. SPELINA KP, COATES DP, MONK CR, PRYS-ROBERTS C, NORLEY I, TURTLE MJ. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. I. Patients premedicated with morphine sulphate. *British Journal of Anaesthesia* 1986; **58**: 1080-4.
7. TAKIZAWA H, GABRA-SANDERS, T, MILLER JD. Analysis of changes in intracranial pressure and pressure-volume index at different locations in the craniospinal axis during supratentorial epidural balloon inflation. *Neurosurgery* 1986; **19**: 1-8.
8. WAGNER JG. A safe method for rapidly achieving plasma concentration plateaus. *Clinical Pharmacology and Therapeutics* 1974; **16**: 691-700.
9. HARTUNG HJ. Beeinflussung des intrakraniellen Druckes durch Propofol (Disoprivan®). Erste Ergebnisse. *Anaesthesist* 1987; **36**: 66-8.
10. STEPHEN H, SONNTAG H, SCHENK HD, KOHLHAUSEN S. Einfluss von Disoprivan (Propofol) auf die Durchblutung und den Sauerstoffverbrauch des Gehirns und die CO₂-Reaktivität der Hirngefäße beim Menschen. *Anesthesist* 1987; **36**: 60-5.
11. SHAPIRO HM, GALINDO A, WYTE SR, HARRIS AB. Rapid intraoperative reduction of intracranial pressure with thiopentone. *British Journal of Anaesthesia* 1973; **45**: 1057-62.
12. MILDE LN, MILDE JH, MICHENFELDER JD. Cerebral functional, metabolic and hemodynamic effects of etomidate in dogs. *Anesthesiology* 1985; **63**: 371-7.
13. BENDTSEN A, KRUSE A, MADSEN JB, ASTRUP J, ROSENORN J, BLATT-LYON B, COLD GE. Use of continuous infusion of althesin in neuroanaesthesia. Changes in cerebral blood flow, cerebral metabolism, the EEG and plasma alphaxalone concentration. *British Journal of Anaesthesia* 1985; **57**: 369-74.

14. FORSTER A, JUDGE O, MOREL D. Effects of midazolam on cerebral blood flow in human volunteers. *Anesthesiology* 1982; **56**: 453-5.
15. GIFFIN JP, COTTRELL JE, SHWIRY B, HARTUNG J, EPSTEIN J, LIM K. Intracranial pressure, mean arterial pressure and heart rate following midazolam or thiopental in humans with brain tumors. *Anesthesiology* 1984; **60**: 491-4.
16. McMOLLUM JSC, DUNDEE JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41**: 995-1000.
17. COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE M. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anaesthesia in humans. *Anesthesia and Analgesia* 1987; **66**: 64-70.
18. WERNER O, MAGNUSSON J, FLETCHER R, CARLSSON C, PETTERSSON KI. Effect of cardioselective β -blockers on the heart rate and arterial pressure responses to laryngoscopy. *Acta Anaesthesiologica Scandinavica* 1982; **26** (Suppl. 76): 78-80.
19. KAUTTO UM. Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 217-21.
20. HAMILL JF, BEDFORD RF, WEAVER DC, COLOHAN AR. Lidocaine before endotracheal intubation: intravenous or laryngotracheal? *Anesthesiology* 1981; **55**: 578-81.
21. STEPHEN H, SONNTAG H, SCHENK HD, KETTLER D, KHAM-BATTA HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; **58**: 969-75.

Effect of propofol on cerebral blood flow and metabolism in man

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Summary

Cerebral blood flow, cerebral oxygen consumption, lactate and glucose metabolism were measured in 13 patients during anaesthesia with nitrous oxide, oxygen and enflurane 0.5% and after 30 minutes infusion of propofol. The mean blood concentration of propofol was 4.06 µg/ml. Cerebral blood flow decreased by 27.6% and cerebral vascular resistance by 51%. There were no changes in lactate and glucose metabolism. Cerebral oxygen consumption decreased by 18.25%. Changes in the electroencephalograph were related to the blood levels of propofol.

Key words

Anesthetics, intravenous; propofol.

Anaesthetics, volatile; enflurane.

Brain; blood flow, glucose, lactate, oxygenation.

There are only few studies on the effect of propofol (2,6-diisopropylphenol) on cerebral blood flow and metabolism in man. Stephen and co-workers¹ found a 51% decrease of cerebral blood flow in patients scheduled for coronary artery bypass surgery after a bolus injection of propofol 2 mg/kg followed by an infusion of 0.2 mg/kg/minute. They noted a proportional decrease of 36% in cerebral oxygen consumption which was associated with a decrease in electroencephalographic (EEG) activity.

We compared cerebral blood flow under stable and comparable conditions of P_{aCO_2} and mean blood pressure – in patients of ASA grade 1 who underwent 35% oxygen in nitrous oxide anaesthesia with enflurane 0.5% before and during a propofol infusion to achieve steady-state anaesthesia.

Methods

Thirteen patients (2 female) aged from 22–62 years scheduled for intervertebral disc surgery were included in the study after informed consent and approval by the hospital ethical committee. No premedication was given. Anaesthesia was induced with thiopentone 5 mg/kg and the patients' tracheas were intubated after pancuronium 0.1 mg/kg. Controlled ventilation of the lungs with 65% nitrous oxide in oxygen and enflurane 0.5% was adjusted to achieve a P_{aCO_2} of 4.8 kPa, controlled by capnography

(capnograph Elema CO₂ Monitor 130) and arterial blood gas analysis.

Monitoring consisted of lead II ECG, Fp1 T5 and Fp2 T6 EEG recording, continuous blood pressure measurement via a radial artery cannula, jugular bulb pressure via a percutaneous catheter (Leder cath 17-gauge), arterial and jugular bulb blood gas, glucose and lactate analysis.

A first CBF measurement was performed when stable conditions were achieved, at least one hour after thiopentone induction, using the xenon 133 inhalation technique. Cerebral radioactivity decay and the expired xenon 133 were recorded by gamma camera (Elscent Apex 215) and cerebral blood flow was calculated using the initial slope index.

An infusion of propofol (three-step infusion technique) was started at a rate of 0.35 mg/kg/minute (21 mg/kg/hour) for 5 minutes after the first CBF measurement, then at 0.2 mg/kg/minute (12 mg/kg/hour) for a further 10 minutes and then at 0.1 mg/kg/minute (6 mg/kg/hour) for the last 25 minutes. This scheme of propofol infusion was based on data collected from a previous personal study of 16 patients where a stable blood concentration of 4 µg/ml was achieved after 30 minutes of infusion.

Blood samples were drawn one minute before the start of the infusion and at 1, 2, 3, 4, 5, 7, 9, 11, 13, 15, 20, 25, 30 and 40 minutes from the jugular bulb, and at 20, 30 and 40 minutes from a peripheral vein. Blood pressure was

Table 1. Experimental conditions. Values expressed as mean (SD).

	Arterial pressure, mmH ₂	Jugular bulb venous pressure, mmHg	Cerebral perfusion pressure, mmHg	Paco ₂ , kPa
Enflurane	74.5 (11.1)	2.6 (2.4)	69.5 (6.9)	4.8 (0.26)
Propofol	77.4 (10.7)	2.8 (2.4)	72.4 (7.6)	4.7 (0.24)

No significant differences between groups.

Table 2. Effects of propofol on cerebral parameters. Values expressed as mean (SD).

	Cerebral blood flow, ml/100g/minute	Cerebral vascular resistance, mmHg/ml/100g/minute	Cerebral metabolic rate for oxygen, ml/100g/minute
Enflurane	51.0 (11.8)	1.41 (0.3)***	3.48 (1.5)
Propofol	36.9 (12.6)*	2.13 (0.8)***	2.88 (1.2)*

*p < 0.05, **p < 0.02, ***p < 0.01, significant differences between groups.

maintained constant with a 0.002% phenylephrine infusion if necessary. A second CBF measurement was done 30 minutes after the start of the infusion under the same conditions of Paco₂ and mean arterial pressure.

Data were submitted to statistical analysis by Student's *t*-test, Wilcoxon's test for paired data and the Kruskal-Wallis test.

Results

All the physiological variables were similar during both CBF measurements: mean arterial pressure, jugular venous pressure and cerebral perfusion pressure remained unchanged (Table 1). The mean cerebral blood flow decreased by 27.6% (*p* < 0.02) in response to propofol infusion, while cerebral vascular resistance increased by 51% (*p* < 0.01) (Table 2). Cerebral oxygen consumption decreased by 18.25% but not significantly; however, this was associated with a decrease in EEG activity.

Cerebral metabolic rates for glucose and lactate did not change significantly during the infusion. The aim of the study was to achieve a high blood concentration of propofol of at least 4 µg/ml, so the patients were divided into three groups according to the depth of anaesthesia based on the EEG recording. There was a correlation (*p* < 0.0001) between propofol blood concentration and EEG changes. However, cerebral blood flow and oxygen consumption did not change significantly between the three groups, despite significantly different blood propofol concentrations.

Discussion

It is difficult to compare the results of this study with those

of other investigators because of variations in measurement and anaesthetic techniques, premedication and the rates of propofol infusion. The infusion technique in this study resulted in a stable blood concentration of propofol (4.06 µg/ml, SD 0.92) within 30 minutes of infusion but there were marked individual variations in blood propofol concentrations despite similar infusion regimens.

The mean cerebral blood flow decreased by 27.6% (*p* < 0.02), less than that reported in the literature, and depended upon the blood concentration. The non-significant decrease of cerebral oxygen consumption was probably due to a lighter level of anaesthesia at the time of the second CBF measurement, as suggested by the EEG trace, despite a mean propofol blood concentration of 4 µg/ml.

Acknowledgments

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References

1. STEPHAN H, SONNTAG H, SCHENK HD, KOHLHAUSEN S. Einfluss von Disoprivan (Propofol) auf die Durchblutung und den Sauerstoffverbrauch des Gehirns und die Co₂-Reaktivität der Hingefäße beim Menschen. Effects of Disoprivan on cerebral blood flow, cerebral oxygen consumption and cerebral vascular reactivity. *Anesthesist* 1987; 36: 60-5.
2. OBRIST WD, THOMPSON HK, WANG HS, WILKINSON WE. Regional cerebral blood flow estimated by Xe 133 inhalation. *Stroke* 1975; 6: 245-56.
3. RISBERG J, ALI F, WILSON EM, WILLS EL, HALSEY JH. Regional cerebral blood flow by Xe 133 inhalation. *Stroke* 1975; 6: 142-8.

Propofol anaesthesia alters somatosensory evoked cortical potentials

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L. A. HERAUT

Summary

This study evaluated the effects of propofol on somatosensory evoked cortical potentials in 20 ASA grade 1 or 2 patients who underwent spinal surgery. Anaesthesia consisted of propofol, dextromoramide, 50% nitrous oxide and oxygen mixture. The induction dose of propofol was 2 mg/kg and was followed by an infusion of 6 mg/kg for the first hour and 3 mg/kg subsequently. Somatosensory evoked cortical potentials were recorded on the scalp and compared to pre-operative values using Student's paired t-test. We observed a significant depression of evoked potential 10 minutes after induction, which continued until the early phase of recovery. Because of its short and quickly reversible action, propofol is an acceptable agent when clinical monitoring of the spinal cord is indicated but is not satisfactory when monitoring has to be based on somatosensory cortical evoked potentials.

Key words

Anaesthetics, intravenous; propofol.

Measurement techniques; somatosensory evoked cortical potentials.

Somatosensory evoked cortical potentials (SECPs) are a useful method for the detection of neurological complications that occur during spinal surgery. However, certain anaesthetic compounds alter SECPs.¹ Propofol is a potentially useful agent for spinal surgery because of its short duration of action and rapid recovery, so it was decided to determine whether propofol *per se* alters SECPs.

Methods

SECPs were studied in 20 patients (mean age 39.5 years, SD 14.5) scheduled to undergo laminectomy where neurological complications were not expected. Patients were classified as ASA grade 1 or 2 and suffered from neither central nor peripheral neurological disorders. All patients were premedicated 2.5 hours before surgery with hydroxyzine 1.5 mg/kg and clorazepate 0.5 mg/kg orally. Anaesthesia was induced with propofol and dextromoramide. The induction dose of propofol was 2 mg/kg followed by an infusion at a rate of 6 mg/kg for the first hour and then 3 mg/kg for the remainder of the procedure. The induction dose of dextromoramide was 0.05 mg/kg followed by 1 mg bolus doses administered according to surgical demand. Patients' lungs were ventilated with nitrous oxide 50% in oxygen.

SECPs were recorded on the scalp with an Fz reference after stimulation of the tibial nerve at the level of the ankle. Control values of SECPs were recorded the day before

surgery. Further values were recorded 2 hours after premedication, 10 minutes after induction and subsequently every 30 minutes. Evoked potentials were recorded in the recovery room every 15 minutes until they returned to a level similar to the control values. Care was taken to keep P_{aCO_2} , temperature and mean arterial blood pressure within normal range.

Student's paired *t*-test was used to determine the statistical significance of differences in latency, amplitude, and both P40 and N50 early wave areas between control and subsequent SECP recordings.

Results

The results are summarised in Table 1. Premedication had no effect on SECPs. However, both the latency and the area of P40 were significantly reduced during anaesthesia and the early phase of recovery.

Discussion

Our results suggest that propofol *per se* does alter SECPs, for several reasons. No change occurred in SECPs after premedication which would indicate that clorazepate and hydroxyzine were the cause. It has been shown that, unlike fentanyl, dextromoramide does not alter SECPs.² Furthermore, Sloan and Koht³ pointed out that nitrous oxide can depress SECPs but it is unlikely that it was responsible

Table 1. SECP evolution during anaesthesia. Values expressed as mean (SD).

	P40 latency, milliseconds	Amplitude, nanovolts	Area
Control (n = 20)	39.8 (3.6)	1.5 (0.8)	12.1 (6.5)
Premedication (n = 20)	40 (3.7)	1.5 (0.8)	11.9 (7)
Induction after 10 minutes (n = 20)	41.1 (3.5)	0.9 (0.6)**	7.7 (1.9)*
Induction after 1 hour (n = 19)	43.9 (4.1)	0.5 (0.4)***	5.3 (2.8)***
Recovery after 15 minutes	43.2 (3.4)	0.9 (0.6)**	8.8 (3.7)*
Recovery after 30 minutes	41.9 (2.9)	1 (0.5)*	11.6 (6.5)

* p < 0.05, ** p < 0.01, *** p < 0.001 compared to control.

for the changes found in this study. Indeed, no change in SECPs was noted in a previous study⁴ in which methohexitone was used rather than propofol in a similar protocol. Whether similar changes in SECPs are induced by propofol when recordings are made from the spinal area instead of the scalp, remains to be established. Moreover, a quantitative relationship between SECP modification and propofol blood concentration has yet to be determined.

References

1. BOYD SG, ROTHWELL JC, COWAN JMA. A method of moni-

toring function in cortico-spinal pathways during scoliosis surgery with a note on motor conduction velocities. *Journal of Neurology, Neurosurgery and Psychiatry* 1986; **49**: 251.
2. PATHAK KS, BROWN FH, CASCORBI HF, NASH CL. Fentanyl and morphine effects on intraoperative somatosensory cortical evoked potentials. *Anaesthesiology* 1982; **57**: A319.
3. SLOAN TB, KOHT A. Depression of cortical somatosensory evoked potentials by nitrous oxide. *British Journal of Anaesthesia* 1984; **57**: 849.
4. DESTRIEATS B, MAURETTE P, CASTAGNERA L, ESPOSITO J, MACOULLARD G, CANTIN P, HERAUT LA. Propofol versus methohexital dans la chirurgie du canal rachidien. *Annales Francaises d'Anesthesie et de Reanimation* 1987; **6**: 301-5.

Propofol infusion and auditory evoked potentials

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Summary

The effects of propofol on auditory evoked potentials (brainstem and middle latency responses) were recorded in six patients. Two different infusion rates were used, 54 and 108 µg/kg/minute. Effects on brainstem responses were not found. Regression of amplitude and latency of middle latency auditory potentials were dose related ($p < 0.01$).

Key words

Anaesthetics, intravenous; propofol.

Measurement techniques; auditory evoked potentials.

The use of intra-operative evoked potentials improves the quality of central nervous system monitoring and gives precise information about both the integrity of sensorial pathways and the effects of anaesthetic drugs on peripheral and central conduction times. Thornton *et al.*^{1–4} showed significant correlations between the latency and amplitude of wave V of brainstem auditory evoked potentials (BAEPs), the latency and amplitude of waves Pa and Nb of middle latency potentials (MLPs) and the use of the intravenous anaesthetic drugs Althesin and etomidate, or the volatile anaesthetics halothane, enflurane and isoflurane. Volatile anaesthetics cause a dose-related regression of BAEPs and MLPs but intravenous anaesthetics cause selective effects: the latencies of BAEP waves are preserved whereas the amplitudes and latencies of waves Pa and Nb of MLPs are affected in a dose-dependent manner.

We performed a preliminary study of the effects of propofol infusions on auditory BAEPs and MLPs in six patients.

Patients and methods

Six patients (3 male) with a mean age of 42 years (SD 7.5) gave informed consent to participate in an investigation approved by the ethical committee of the Medical School of the University of Naples. The three male patients underwent haemorrhoidectomy and the three female patients, varicectomy.

Premedication with intramuscular fentanyl 2 µg/kg, droperidol 100 µg/kg and atropine 8 µg/kg was followed after 45 minutes by induction of anaesthesia with propofol. The trachea was intubated 3 minutes after induction aided by pancuronium 0.1 mg/kg and the lungs ventilated with

66% nitrous oxide in oxygen. Intermittent positive pressure ventilation was adjusted to deliver a tidal volume of 10–12 ml/kg at a frequency of 12 breaths/minute. The fresh gas flow was adjusted to maintain the end tidal carbon dioxide in the range 5–5.8 kPa. A continuous infusion of propofol delivered by a calibrated syringe pump, was started immediately after induction at either 54 or 108 µg/kg/minute (each infusion period lasted for 30 minutes).

Monitoring in all patients was carried out by ECG, digital plethysmography (Sirecust Siemens BS1) and capnography. Arterial pressure was monitored by automatic oscillotonometer, oesophageal temperature was measured with a thermistor probe. Auditory evoked responses were recorded by Basis EPM (Ote Biomedica) before induction of anaesthesia and 20 minutes after the start of propofol infusion at 54 µg/kg/minute (T_1) or 108 µg/kg/minute (T_2). Electrodes were placed at EEG positions A_1 , A_2 (positives), C_z (negative) Nasion (ground at no-cephalic point). Alternate binaural clicks were applied with simultaneous recording (number average 2048). Times of analysis were 10 milliseconds for BAEPs and 50 milliseconds for MLPs. Data was recorded at a sensitivity of 5 µV/DIV with a low frequency cut-off filter at 100 Hz and high frequency cut-off at 2 kHz. Stimulation data were for periods of 0.05 seconds (BAEPs) and 10 seconds (MLP) with a duty cycle of 0.10 milliseconds at an intensity of 90 ± 2 dB.

The latencies (milliseconds) of waves I, III and V, the amplitude (µV) of wave V and the interpeak intervals I–III, I–V and III–V were examined for BAEPs, and the latencies and amplitudes of waves Pa and Nb for MLPs. Statistical analyses were carried out by Student's *t*-test ($p < 0.05$ was considered to indicate statistical significance).

Haemodynamic changes were recorded after induction,

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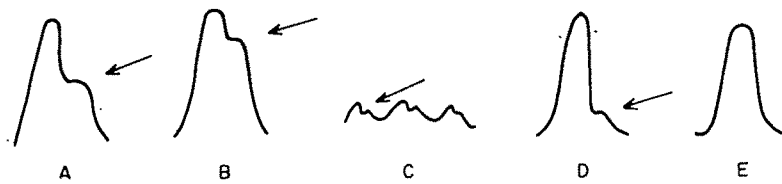


Fig. 1. Plethysmographic pattern scores. A, Normal (0 points); B, increase of dicotic wave (–1 point); C, marked reduction of amplitude (–2 points); D, reduction of dicotic wave (+1 point); E, lack of dicotic wave with peripheral vasodilatation (+2 points).

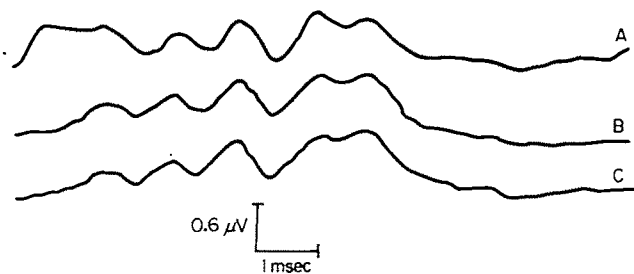


Fig. 2. BAEPs patterns. A, Baseline; B, during propofol infusion at 54 µg/kg/minute; C, during propofol infusion at 108 µg/kg/minute.

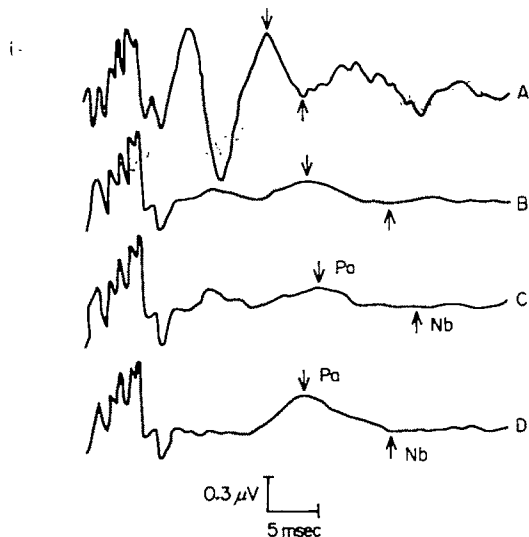


Fig. 3. MLP patterns. A, Baseline; B, during propofol infusion at 54 µg/kg/min; C, during propofol infusion at 108 µg/kg/minute; D, 5 minutes after end of propofol infusion.

during tracheal intubation and during the two propofol infusions under surgical stress; particular attention was paid to changes in heart rate, diastolic and systolic arterial pressures, rate–pressure product and plethysmographic patterns (for these we used the scoring system shown in Fig. 1). Student’s *t*-test and the Chi-squared test were used for statistical analysis of haemodynamic changes.

Results

Table 1 shows the variation in the interpeak intervals I–III and III–V for BAEPs (Fig. 2). The only statistically significant change was the difference between the latency of wave I during propofol infusion at 108 µg/kg/minute 1.64

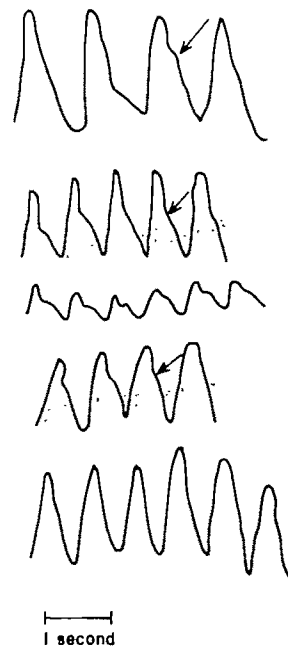


Fig. 4. Plethysmographic patterns (Dicotic waves are indicated by arrows). A, Baseline; B, 30 seconds after induction; C, 15 seconds after intubation; D, during propofol infusion at 54 µg/kg/minute; E, during propofol infusion at 108 µg/kg/minute.

(SD 0.12) and the basal value, 1.49 (SD 0.08). Table 2 shows the changes in MLPs. The shift of waves Pa and Nb and the regression of peak-to-peak amplitudes are statistically significant and dose related (Fig. 3).

There were no significant haemodynamic changes (heart rate, systolic and diastolic pressure, rate–pressure product) (Table 3). Analysis of the plethysmographic patterns, however, showed an irregular distribution (*p* < 0.05) during induction and intubation, when patterns that suggested respectively vasodilatation and vasoconstriction were predominant (Table 4, Fig. 4).

Discussion

The propofol infusion rates that we used are in accordance with the clinical experimental protocol of Coates *et al.*⁵ Our study demonstrates the importance of a comparative evaluation of plethysmographic patterns when haemodynamic changes are assessed. Analysis of changes in variables often does not enable significant alterations to be noticed, particularly during intubation or surgical stress.^{6–8}

Propofol has a selective effect in that BAEPs are pre-

Table 1. Variation of BAEPs during propofol infusion. Values expressed as mean (SD).

	Control	Propofol 54 µg/kg/minute	Propofol 108 µg/kg/minute
Latency, milliseconds			
I wave	1.49 (0.08)	1.59 (0.12)	1.64 (0.12)*
III wave	3.72 (0.08)	3.77 (0.07)	3.79 (0.12)
V wave	5.63 (0.08)	5.68 (0.16)	5.68 (0.16)
Amplitude, µV			
V wave	0.52 (0.18)	0.66 (0.53)	0.65 (0.54)
Interpeak latency, milliseconds			
I-III	2.23 (0.05)	2.22 (0.16)	2.15 (0.12)
III-V	1.92 (0.09)	1.91 (0.09)	1.90 (0.13)
I-V	4.13 (0.1)	4.09 (0.18)	4.05 (0.20)

* p < 0.05 compared with control.

Table 2. MLP changes. Values expressed as mean (SD).

	Baseline	Propofol 54 µg/kg/minute	Propofol 108 µg/kg/minute
Pa latency, milliseconds	20.34 (1.76)	24.78 (2.24)*	25.74 (2.12)*
Nb latency, milliseconds	28.60 (2.9)	36.26 (2.5)**	37.28 (2.5)**
Amplitude, µV (peak to peak)	1.63 (0.8)	0.31 (0.13)**†	0.14 (0.1)**†

* p < 0.05, compared to baseline.

** p < 0.01.

† p < 0.05 compared to propofol 108 µg/kg/minute.

Table 3. Haemodynamic changes. Values expressed as mean (SD).

	Baseline	30 seconds after induction	15 seconds after intubation	Propofol 58 µg/kg/minute	Propofol 108 µg/kg/minute
Heart rate, beats/minute	75.6 (5.8)	80.3 (4.6)	79.3 (7.1)	77.5 (5.2)	78.3 (6.3)
Systolic pressure, mmHg	122 (14.3)	111 (16.2)	135 (37.4)	118 (28)	115 (23)
Diastolic pressure, mmHg	78 (8)	74 (10)	88 (16)	79 (18)	80 (15)
Rate-pressure product	9178 (993)	8900 (1356)	10695 (2973)	9168 (2050)	8971 (1418)

Table 4. Distribution of plethysmographic patterns during propofol infusion ($\chi^2 = 29.52 < 0.05$).

	Plethysmographic pattern (Fig. 1)				
	A	B	C	D	E
Baseline	50%	34%	—	16%	—
30 seconds after induction	34%	—	—	50%	16%
15 seconds after intubation	—	34%	50%	16%	—
Propofol infusion 54 µg/kg/minute	34%	—	—	66%	—
Propofol infusion 108 µg/kg/minute	16%	—	—	50%	34%

See also Fig. 4.

served whilst MLPs are affected in a dose-dependent manner similar to the effect of Althesin and etomidate.^{2,3} Halogenated anaesthetic agents, which depress both BAEPs and MLPs cause significant dose-related haemodynamic changes. By contrast, drugs that depress only MLPs cause less haemodynamic changes. The increase in wave I noted in Table 1 is related to the use of nitrous oxide^{9,10}.

An anaesthetic technique based on propofol supplemented with 66% nitrous oxide in oxygen appears to be safe and satisfactory in the light of the results of this preliminary study. This technique does not affect BAEPs so it can be

used in neurosurgery or vascular surgery, when it is necessary to preserve the integrity of BAEPs. The observed changes in the plethysmographic patterns indicate that only high infusion rates (108 µg/kg/minute) ensure a satisfactory microcirculation.

References

1. THORNTON C, HENEGHAN CPH, JAMES MFM, JONES JG. Effects of halothane and enflurane with controlled ventilation on auditory evoked potentials. *British Journal of Anaesthesia* 1984; **56**: 315-23.

2. THORNTON C, HENEGHAN CPG, NAVARATNARAJAH M, JONES JG. Selective effects of Althesin on the auditory evoked response in man. *British Journal of Anaesthesia* 1986; **58**: 422-7.

3. THORNTON C, HENEGHAN CPH, NAVARATNARAJAH M, BATEMAN PE, JONES JG. Effect of etomidate on the auditory evoked response in man. *British Journal of Anaesthesia* 1985; **57**: 554-61.

4. HENEGHAN CPH, THORNTON C, NAVARATNARAJAH M, JONES JG. Effects of isoflurane on the auditory evoked response in man. *British Journal of Anaesthesia* 1987; **59**: 277-82.

5. COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE M. Haemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anaesthesia in humans. *Anaesthesia and Analgesia* 1987; **66**: 64-70.

6. NUBOER JA, DORLAS JC, SALT PJ. The effect of ketamine on the peripheral circulation: a possible sympathetic ganglion blocking effect. *European Journal of Anaesthesiology* 1986; **3**: 143-58.

7. DORLAS JC, NUBOER JA. Photo-electric plethysmography as a

- monitoring device in anaesthesia. Application and interpretation. *British Journal of Anaesthesia* 1985; **57**: 524-30.
8. NUBOER JA, DORLAS JC. Comparison of plethysmograms taken from finger and pinna during anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 531-4.
9. CUOCOLO R, AMANTEA B, CASSANDRA, SAVOIA G, SEQUINO L, TUFANO R. Evaluation of evoked cortical potentials during the administration of some anesthetics and related drugs. In: TIENG M, COUSINS MJ, eds. *Pharmacological basis of anesthesiology: clinical pharmacology of new analgesics and anesthetics*. Raven Press: New York, 1983: 199-206.
10. SAVOIA G, AMANTEA B, ESPOSITO C, BELFIORE F, CUOCOLO R. I potenziali evocati acustici e somatosensoriali in anestesia. *Minerva Anestesiologica* 1985; **51**: 191-202.

Comparison of propofol and methohexitone anaesthesia for thermocoagulation therapy of trigeminal neuralgia

J. KYTTÄ AND P. H. ROSENBERG

Summary

Propofol and methohexitone given in equipotent doses were compared for anaesthesia for thermocoagulation of trigeminal rootlets. Thirty-eight patients received two to six injections of the induction agents in one therapy session. The increase in arterial blood pressure during coagulation was significantly lower in the propofol group. Respiratory problems were encountered more often in those who received methohexitone (7/19 patients) than propofol (2/19 patients). There was a small but significant increase in blood propofol concentrations as well as in methohexitone plasma concentrations after repeated injections. Individual wake-up times increased to a statistically significant extent in relation to the number of doses of the induction agent but the increases were clinically unimportant (maximal mean change approximately 2 minutes). There were no differences in wake-up times between the two anaesthetic groups.

Key words

Anaesthetic techniques, regional; trigeminal.

Anaesthetics, intravenous; propofol, methohexitone.

Thermocoagulation therapy for the treatment of trigeminal neuralgia requires the patient to be woken up and anaesthesia re-induced several times, at intervals of 20–30 minutes.¹ The treatment involves placement of the needle and thermocoagulation at increasing temperatures. The result of each coagulation is carefully assessed each time the patient awakens in order to ensure optimal lesion of the nerve rootlets, before anaesthesia is re-induced. Methohexitone has been used routinely for this procedure in many neurosurgical centres.

The commonest problems that arise during thermocoagulation therapy are difficulty in maintenance of a patent airway and extreme elevation of the arterial blood pressure. The use of methohexitone was associated with sudden episodes of hypertension in a study by Sweet *et al.*² Propofol may prove to be a more suitable anaesthetic agent for this procedure because of its hypotensive action³ and shorter recovery time.⁴ The present study compared propofol and methohexitone in terms of haemodynamics, respiration and side effects in patients who underwent thermocoagulation therapy.

Methods

The haemodynamic, respiratory and possible side effects of propofol and methohexitone were studied in 38 patients of ASA grades 1–3 scheduled for thermocoagulation of the trigeminal nerve rootlets. Allocation to the two drugs was

at random and all patients gave their consent to the study which was approved by the ethical committee of the hospital.

A cannula was placed into a large cubital vein, and one of the radial arteries was cannulated for arterial blood pressure measurement and blood sampling. Oxygen 4 litres/minute was given through a nasal catheter throughout the procedure. The ECG was monitored continuously using the CM₅ lead. The patients were premedicated with atropine 0.01 mg/kg.

The anaesthetic agent was administered into a rapidly running infusion. The initial induction dose of propofol ranged from 1.5–2.5 mg/kg and that of methohexitone from 0.8–1.5 mg/kg. The doses given at approximately 20-minute intervals for subsequent anaesthesia were adjusted slightly as required. Thermocoagulation (60–90°C) was performed for 1 minute after loss of the eyelash reflex. All coagulation procedures were carried out by the same neurosurgeon. Side effects were recorded during and immediately after anaesthesia; blood samples were drawn 3 minutes after induction for blood gas analysis. Additional blood samples were drawn on opening of the eyes in roughly half of the patients, for high-performance liquid chromatography assays of blood propofol⁵ or methohexitone plasma concentration.⁶ The wake-up time and times to orientation in time and place were recorded after each period of anaesthesia. A 12-lead ECG was recorded pre-operatively and on the first postoperative day.

Table 1. Characteristics of 38 patients given intravenous propofol or methohexitone for induction of anaesthesia. Values expressed as mean (SD).

	Sex, M/F	Age, years	Weight, kg	Height, cm	ASA grade		
					1	2	3
Propofol	6/13	60 (14)	72 (15)	166 (8)	5	8	6
Range		36–86	50–100	150–182			
Methohexitone	10/9	60 (12)	75 (15)	167 (10)	4	11	4
Range		41–75	50–105	150–183			

Four patients in each group were on antihypertensive medication.

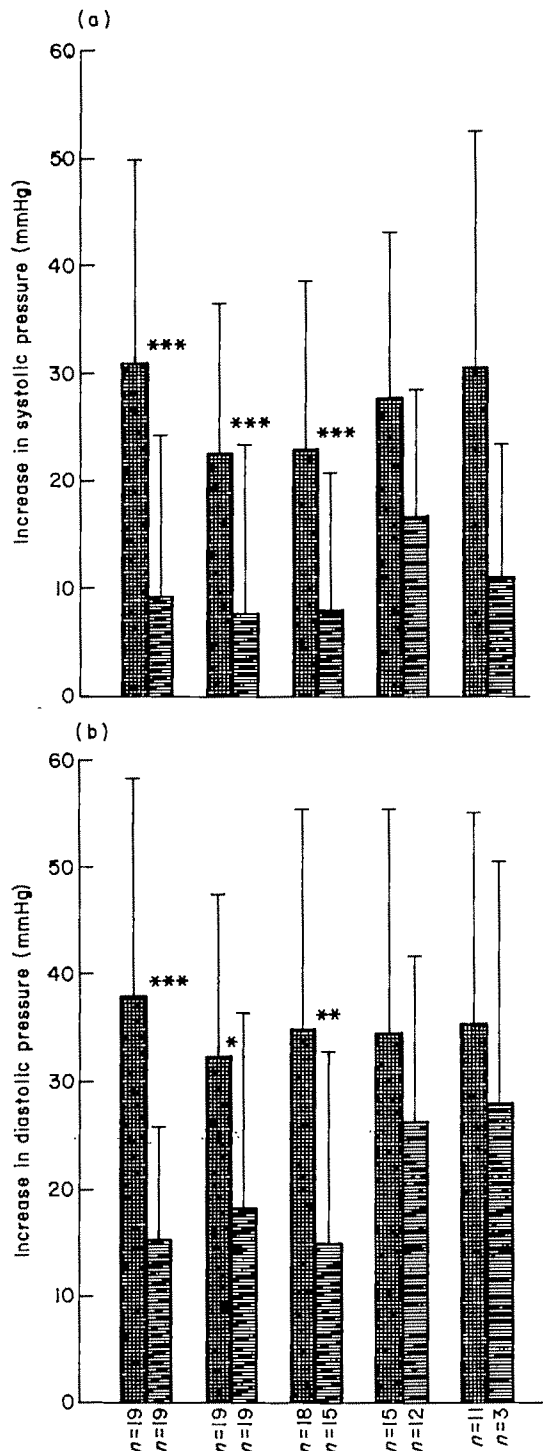


Fig. 1. Mean maximal changes in (a) systolic and (b) diastolic arterial blood pressure (mmHg) during thermocoagulation after each dose of drug. Standard deviation bar is shown in only one direction. ▨, Methohexitone; ■, propofol; n, number of patients.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Statistical analysis. The *t*-test and Chi-squared test were used to evaluate differences in haemodynamic changes, propofol blood concentrations and side effects.

Results

Patient characteristics are shown in Table 1. The two groups were comparable for age, weight and height. Each patient received at least two, but not more than six periods of anaesthesia in one thermocoagulation session.

The dose of propofol needed for loss of the eyelash reflex in each of the repeated anaesthetics ranged from 1.5–3.4 mg/kg (mean 1.8 mg/kg) and the dose of methohexitone from 0.8–2.7 mg/kg (mean 1.2 mg/kg). Heart rate changes were similar in both groups. The mean elevations of systolic and diastolic arterial blood pressures were greater (systolic, $p < 0.001$; diastolic, $p < 0.05$) in the methohexitone group (Fig. 1), in which extremely high blood pressure elevations

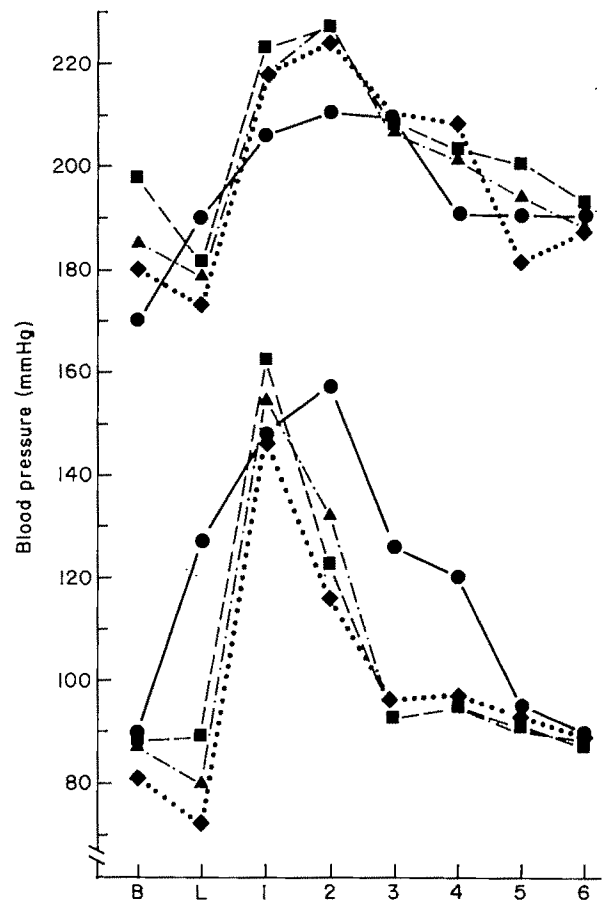


Fig. 2. Systolic and diastolic arterial blood pressure during methohexitone anaesthesia and thermocoagulation in one particular patient, who was treated twice at a one-week interval. B, Just before anaesthesia; L, lowest value before treatment. —, Needle; ---, 70°C; ·····, 80°C; — · — ·, 90°C.

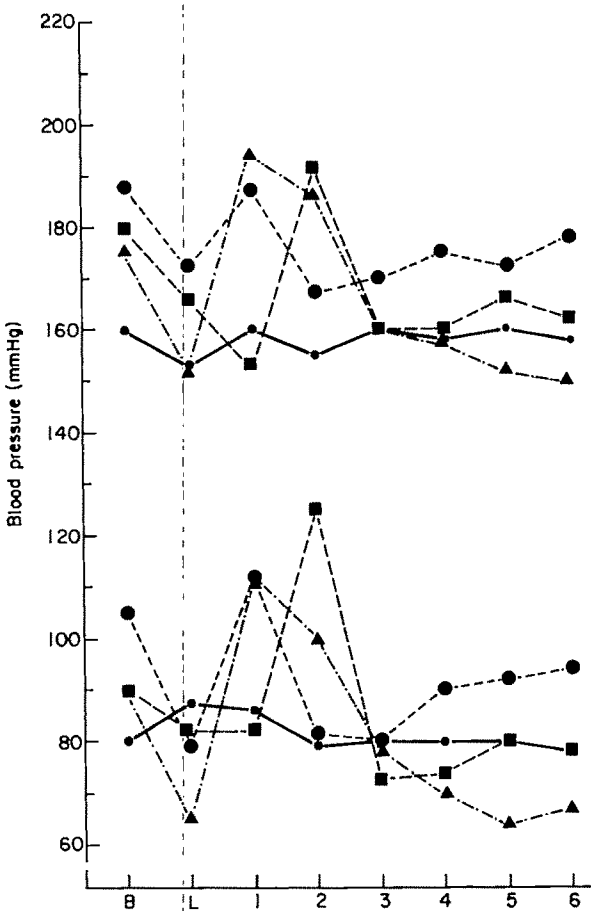


Fig. 3. Systolic and diastolic arterial blood pressure during propofol anaesthesia one week later in the same patient shown in Fig. 2. B, Just before anaesthesia; L, lowest value before treatment. —, Needle; ---, 70°C; - · - · -, 80°C; · · · · ·, 90°C.

of up to 223/162 mmHg were recorded on occasion. The maximum blood pressure recorded in the propofol group during coagulation was 190/125 mmHg. It is interesting that the extreme values with methohexitone and propofol occurred in the same patient who underwent trigeminal nerve rootlet coagulations at a one-week interval (Figs 2 and 3). Antihypertensive medication (alpha- or beta-sympatholytic) had to be given to five patients, all in the methohexitone group.

Upper airway obstruction occurred in one patient in the propofol group and in six patients who received methohexitone; tongue traction relieved the obstruction. One patient who received propofol was apnoeic for approximately one minute and another patient with multiple sclerosis in the methohexitone group required ventilation via a facemask for approximately 9 minutes after the fourth dose. Five patients in the methohexitone group had hiccoughs.

The results of arterial blood gas analyses were normal and similar regardless of the drug used. Oxygen saturation did not decrease below 85% in any patient. ST depression was noted in two patients in the methohexitone group and multifocal extrasystoles in one. There were no persistent differences between the ECG on the first postoperative day and that prior to the operation.

The mean blood concentrations of propofol and plasma concentrations of methohexitone are shown in Table 2. There was a slight increase ($p < 0.05$) in mean propofol levels (2.4 µg/ml 3 minutes after the fourth anaesthetic

Table 2. Blood propofol and plasma methohexitone concentrations after repeated doses. Values expressed as mean (SD).

	Propofol	n	Methohexitone	n
<i>1st dose</i>				
Dose, mg/kg	1.8 (0.3)	13	1.3 (0.4)	9
Concentration at 3 minutes, µg/ml	1.77 (1.20)	13	2.18 (0.69)	9
Time from injection to opening of eyes, minutes	5.3 (1.5)	11	5.4 (0.7)	8
Concentration at opening of eyes, µg/ml	0.78 (0.40)	11	1.46 (0.90)	9
<i>2nd dose</i>				
Dose, mg/kg	1.8 (0.3)	13	1.4 (0.5)	9
Concentration at 3 minutes, µg/ml	2.03 (1.14)	13	3.19 (1.39)	9
Time from injection to opening of eyes, minutes	6.1 (1.7)	12	6.0 (0.7)	9
Concentration at opening of eyes, µg/ml	1.02 (0.70)	12	1.63 (0.78)	9
<i>3rd dose</i>				
Dose, mg/kg	1.8 (0.3)	10	1.1 (0.1)	7
Concentration at 3 minutes, µg/ml	2.53 (0.30)	10	3.38 (1.48)	7
Time from injection to opening of eyes, minutes	6.8 (2.0)	9	6.4 (0.7)	7
Concentration at opening of eyes, µg/ml	1.04 (0.48)	9	1.91 (0.95)	7
<i>4th dose</i>				
Dose, mg/kg	1.8 (0.3)	8	1.2 (0.1)	5
Concentration at 3 minutes, µg/ml	2.38 (1.06)	8	3.71 (1.37)	4
Time from injection to opening of eyes, minutes	7.2 (1.9)	7	7.6 (1.6)	5
Concentration at opening of eyes, µg/ml	1.19 (0.44)	7	1.98 (0.97)	5

versus 1.8 µg/ml after the first), and in mean methohexitone (3.7 µg/ml versus 2.2 µg/ml, respectively), associated with the repeated doses of the induction agents.

Wake-up times were similar in both groups (Table 3) but wake-up times and time to orientation increased slightly after the repeated anaesthetics and the changes were statistically significant (Table 3).

Discussion

The high and sudden arterial blood pressure elevations which occurred in the methohexitone group may constitute a serious risk, for example, to the myocardial oxygen balance. In fact, clinical judgment warranted pharmacological intervention in five patients. The arterial pressure elevations would probably have been smaller if larger doses of methohexitone had been used, although this might have resulted in an increased frequency of respiratory problems and prolonged recovery. An analgesic added to the barbiturate might attenuate the hypertensive reaction but would obscure sensory testing. Propofol reduces systemic vascular resistance⁷ and cardiac output⁸ and, in the present study, provided smoother haemodynamic conditions than methohexitone. Propofol may possess some analgesic properties⁹ but the increase in arterial blood pressure at the time of coagulation was not totally arrested.

Table 3. Wake-up times and time to orientation after repeated doses of propofol or methohexitone. Values expressed as mean (SD).

	1st dose			2nd dose			3rd dose			4th dose			5th dose	
	Dose, mg/kg	Wake-up, minutes	Orientation, minutes	Dose, mg/kg	Wake-up, minutes	Orientation, minutes	Dose, mg/kg	Wake-up, minutes	Orientation, minutes	Dose, mg/kg	Wake-up, minutes	Orientation, minutes	Orientation, minutes	
Propofol	1.9 (0.5)	5.1 (1.4)	6.4 (1.7)	1.9 (0.5)	6.2 (1.5)	7.3 (1.7)	1.9 (0.5)	7.0 (1.8)	8.5 (2.1)	1.8 (0.3)	7.2 (1.5)	8.7 (2.3)	8.0 (2.6)	
n	19	19	19	19	19	19	15	15	15	12	12	11	3	
Methohexitone	1.2 (0.4)	5.2 (0.9)	6.5 (1.4)	1.2 (0.4)	5.5 (1.1)	6.7 (1.2)	1.2 (0.4)	6.1 (1.4)	7.8 (2.2)	1.2 (0.2)	6.8 (2.1)	8.1 (2.5)	8.8 (2.7)	
n	19	19	19	19	19	19	18	18	18	15	15	15	11	

*p < 0.01, **p < 0.001 versus first dose; ***p < 0.05.

Propofol appeared to be safer than methohexitone with respect to upper airway obstruction, and respiratory depression did not pose a problem, probably because of the strong pain stimulus.

The pharmacokinetic profile of propofol ($T_{1/2\beta}$ 45 minutes, $T_{1/2\gamma}$ 300 minutes) suggests that an increase in the blood concentration of propofol is only to be expected after repeated anaesthesia.¹⁰ This coincided with a small (<2 minutes) increase in the wake-up time after consecutive doses. There was also some accumulation of methohexitone in the plasma after closely repeated doses despite the rapid plasma clearance and relatively fast metabolism of this barbiturate.¹¹ The recovery time with this anaesthetic increased slightly with increasing number of doses.

We conclude that compared with methohexitone, propofol is a clinically safer anaesthetic for patients who undergo thermocoagulation of trigeminal rootlets.

Acknowledgments

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References

1. SWEET WH, WEPSIC JG. Controlled thermocoagulation of trigeminal ganglion and rootlets for differential destruction of pain fibers. Part I. Trigeminal neuralgia. *Journal of Neurosurgery* 1974; **39**: 143–56.
2. SWEET WH, POLETTI CE, ROBERTS JT. Dangerous rises in blood pressure upon heating of trigeminal rootlets; increased bleeding times in patients with trigeminal neuralgia. *Neurosurgery* 1985; **17**: 843–4.
3. KAY B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41**: 589–95.
4. ADAM HK, BRIGGS LP, BAHAR M, DOUGLAS EJ, DUNDEE JW. Pharmacokinetic evaluation of ICI 35 868 in man. Single induction doses with different rates of injection. *British Journal of Anaesthesia* 1983; **55**: 97–103.
5. ADAM HK, DOUGLAS EJ, PLUMMER GF, COSGRAVE MB. Estimation of ICI 35 868 (Diprivan®) in blood by high performance liquid chromatography following coupling with Gibb's reagent. *Journal of Chromatography* 1981; **223**: 232–7.
6. BÜCH HP, BÜCH U, ALTMAYER P. A simple, rapid and sensitive thiopental assay in serum and its application for clinical research. In: BERGMAN H, KRAMAR H, STEINBEREITHNER K, eds. *VIIth European Congress of Anaesthesiology, Abstracts, Vol. 16*. Vienna: Verlag Wilhelm Maudrich, 1986; 377.
7. GROUNDS RM, MORGAN M, LUMLEY J. Some studies on the properties of the intravenous anaesthetic, propofol ('Diprivan')—a review. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 90–5.
8. PRYS-ROBERTS C, DAVIES JR, CALVERLEY RK, GOODMAN NW. Haemodynamic effects of infusions of diisopropyl phenol (ICI 35 868) during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1983; **55**: 105–11.
9. BRIGGS LP, DUNDEE JW, BAHAR M, CLARKE RSJ. Comparison of the effect of diisopropyl phenol (ICI 35 868) and thiopentone on response to somatic pain. *British Journal of Anaesthesia* 1982; **54**: 307–11.
10. COCKSHOTT ID, BRIGGS LP, DOUGLAS EJ, WHITE M. Pharmacokinetics of propofol in female patients: studies using single bolus injections. *British Journal of Anaesthesia* 1987; **59**: 1103–10.
11. HUDSON RJ, STANSKI DR, BURCH PG. Pharmacokinetics of methohexital and thiopental in surgical patients. *Anesthesiology* 1983; **59**: 215–19.

Intra-ocular pressure changes during induction of anaesthesia and tracheal intubation

A comparison of thiopentone and propofol followed by vecuronium

R. K. MIRAKHUR, P. ELLIOTT, W. F. I. SHEPHERD AND D. B. ARCHER

Summary

Intra-ocular pressure was measured during induction of anaesthesia with propofol (n = 40) or thiopentone (n = 40) followed by vecuronium to facilitate tracheal intubation which was carried out 3 minutes after the administration of relaxant. The average induction doses were 2.15 and 4.83 mg/kg for propofol and thiopentone, respectively. Half the patients in each group received a supplementary dose of the same induction agent (propofol 1.0 mg/kg or thiopentone 2.0 mg/kg) prior to intubation. Both propofol and thiopentone produced a significant reduction in intra-ocular pressure which decreased further after administration of vecuronium as well as the second smaller dose of the induction agents. Intra-ocular pressure prior to intubation was lower in the two propofol groups in comparison to the corresponding thiopentone groups. Intubation was associated with an increase in intra-ocular pressure but it still remained significantly below the baseline values except in the group given one dose of thiopentone. Supplementary doses of induction agents before intubation attenuated the increase in intra-ocular pressure. Propofol was significantly more effective in this respect and this group showed the lowest intra-ocular pressure throughout the study period. However, administration of propofol resulted in a 30% incidence of pain on injection and a decrease in systolic arterial pressure of more than 30% in about half the patients.

Key words

*Anaesthetics, intravenous; propofol, thiopentone.
Measurement techniques; intra-ocular pressure.*

Propofol (2,6-di-isopropylphenol) is a new intravenous anaesthetic agent whose use is associated with a rapid and smooth induction of anaesthesia and a rapid and smooth recovery.^{1–4} Good control of intra-ocular pressure (IOP) during induction and maintenance of anaesthesia is essential for the success of intra-ocular surgery, and propofol produces a significant and somewhat greater reduction in IOP than thiopentone.^{5,6} A second, smaller dose of propofol given just prior to intubation attenuates the increase in IOP associated with this manoeuvre when it is facilitated with suxamethonium.⁶ It is likely that the increase in IOP would be less if a non-depolarising relaxant rather than suxamethonium were used to facilitate intubation. The present study compared IOP changes after induction of anaesthesia with thiopentone and propofol followed by vecuronium to facilitate tracheal intubation. The effect of a second, smaller dose of the induction agents immediately prior to intubation was also investigated.

Methods

Eighty adult patients 18–80 years old were included in the study after their informed consent and approval from the

ethical committee were obtained. All conformed to ASA grade 1 or 2 and were scheduled to undergo elective ophthalmic surgery under general anaesthesia. Patients with pre-existing elevated IOP (glaucoma), hypertension or obesity were not studied.

All patients were premedicated with diazepam 5–10 mg orally 60–90 minutes pre-operatively and anaesthesia was induced with a sleep dose of either propofol (60 patients) or thiopentone (40 patients) preceded by fentanyl 100 µg. Adequacy of induction was ascertained by loss of the eyelash reflex and failure to respond to verbal communication. Vecuronium 0.1 mg/kg was administered to provide muscle relaxation and to facilitate tracheal intubation and patients' lungs were ventilated with 66% nitrous oxide in oxygen. The trachea was intubated 3 minutes after administration of vecuronium. Half the patients in each group received an additional, smaller dose of the same induction agent, i.e. propofol 1.0 mg/kg or thiopentone 2.0 mg/kg one minute prior to intubation. The allocation of patients to the four groups was randomised.

Intra-ocular pressure was measured with a hand-held applanation tonometer in the eye not to be operated upon. Baseline (control) IOP was measured before the induction

of anaesthesia after instillation of 1.0% amethocaine. Measurements of IOP were made after the administration of the induction agent, before intubation (i.e. after the administration of vecuronium and the additional dose of the induction agent in those who received it), immediately after intubation and cuff inflation and 1 and 2 minutes later, when the study was terminated and further anaesthesia maintained with the addition of isoflurane. Heart rate and systolic arterial pressure were recorded at the same times as the IOP using an ECG and a Dinamap. End tidal carbon dioxide was measured with a capnograph. The occurrence of side effects such as involuntary movements, tremor, hiccough and pain on injection were noted and used to grade the induction as good, adequate or poor depending upon whether there were no, minor or severe side effects.

The results were subjected to analysis of variance and *t*-tests.

Results

The ages, weights and the baseline IOPs were comparable in the four groups (Table 1) with no significant differences. The induction doses of propofol and thiopentone were 2.15 mg/kg (SD 0.43) and 4.83 mg/kg (SD 0.73), respectively. The induction agents were administered into a vein on the dorsum of the hand in the majority of patients (38 and 37 out of 40 for propofol and thiopentone, respectively).

Intra-ocular pressure during induction in the four groups are shown in Table 2 and the percentage changes are shown in Fig. 1. Administration of both propofol and thiopentone resulted in a significant reduction in IOP ($p < 0.001$) which averaged about 42% in those given propofol and about 36% in those given thiopentone. The differences between the groups were, however, insignificant. There was a further reduction in IOP measured before intubation. The difference between the single dose propofol and the single dose thiopentone groups was significant at this time ($p < 0.01$). There was neither significant difference between the two groups that received the supplementary doses of the induction agents, nor between single and supplementary dose groups with the same induction agent.

The IOP increased significantly ($p < 0.01$) as a result of intubation, in comparison to the values immediately before intubation, but was still below the baseline values in all groups and significantly so ($p < 0.01$) except in the group that received the single dose of thiopentone. Analysis of variance showed significant differences between the groups at this time ($p < 0.01$). This was due to significantly lower IOP in the propofol group in comparison to the thiopentone group ($p < 0.05$) and to significantly lower IOP in those who received the supplementary doses in comparison to those who received only a single dose of each of the two induction agents ($p < 0.05$ to $p < 0.005$). The group that received the supplementary dose of propofol showed the

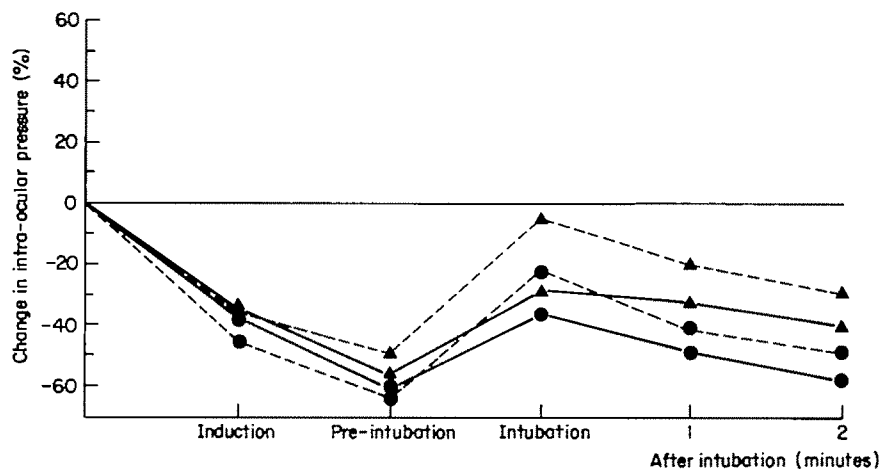


Fig. 1. Percentage changes in intra-ocular pressure during induction of anaesthesia and tracheal intubation. ●—●, Propofol; ○---○, propofol with supplement; ▲—▲, thiopentone; △---△, thiopentone with supplement.

Table 1. Age, weight and baseline intra-ocular pressure (IOP). Values expressed as mean (SD).

	Propofol	Propofol with supplement	Thiopentone	Thiopentone with supplement
Age, years	63 (13.5)	58 (18.1)	63 (14.6)	67 (13.0)
Weight, kg	65 (15.7)	64 (14.8)	67 (10.2)	66 (14.2)
Baseline IOP, mmHg	14.6 (2.46)	15.1 (4.11)	13.5 (3.79)	14.3 (4.58)

Table 2. Mean (SD) intra-ocular pressure in mmHg during induction of anaesthesia and tracheal intubation.

	Baseline	Induction	Before intubation	Intubation	1 minute after intubation	2 minutes after intubation
Propofol	14.6 (2.46)	8.1 (2.83)**	5.3 (2.13)**	11.5 (2.56)**	8.4 (2.56)**	7.5 (2.48)**
Propofol with supplement	15.1 (4.11)	9.4 (3.90)**	5.9 (3.21)**	9.7 (4.19)**	7.8 (3.55)**	6.6 (3.37)**
Thiopentone	13.5 (3.79)	8.6 (2.98)**	6.9 (2.67)**	12.8 (4.51)	10.8 (3.77)*	9.6 (3.32)*
Thiopentone with supplement	14.3 (4.58)	9.1 (3.78)**	6.2 (3.19)**	10.3 (4.12)*	9.6 (4.0)*	8.6 (3.88)**

* $p < 0.05$, ** $p < 0.001$ in comparison to the respective baseline.

Table 3. Mean (SD) systolic arterial pressure in mmHg during induction and tracheal intubation.

	Baseline	Induction	Before intubation	Intubation	1 minute after intubation	2 minutes after intubation
Propofol	154 (20.1)	126 (23.4)**	109 (27.4)**	133 (27.9)*	135 (27.1)*	125 (26.4)**
Propofol with supplement	151 (23.4)	132 (16.8)*	107 (16.9)**	129 (23.9)**	126 (27.1)**	118 (22.7)**
Thiopentone	156 (20.2)	134 (23.9)**	129 (28.0)**	157 (28.2)	162 (34.3)	153 (33.8)
Thiopentone with supplement	158 (20.9)	141 (23.5)**	127 (23.9)**	144 (29.5)	150 (27.9)	142 (24.2)*

* p < 0.05, ** < p < 0.001 in comparison to the respective baseline.

Table 4. Mean (SD) heart rates in beat/minute during induction and tracheal intubation.

	Baseline	Induction	Before intubation	Intubation	1 minute after intubation	2 minutes after intubation
Propofol	81 (16.6)	81 (15.0)	74 (16.3)*	81 (18.1)	79 (18.2)	76 (17.4)*
Propofol with supplement	77 (18.6)	83 (15.5)	72 (11.0)	82 (15.2)	81 (15.6)	79 (15.3)
Thiopentone	74 (14.1)	82 (10.9)*	74 (10.1)	90 (13.5)**	86 (12.2)**	82 (11.0)*
Thiopentone with supplement	81 (11.9)	83 (12.2)	76 (9.0)	89 (14.8)*	87 (14.5)*	83 (13.3)

* p < 0.05, ** < p < 0.001 in comparison to the respective baseline.

Table 5. Side effects.

	Propofol (n = 40)	Thiopentone (n = 40)
Pain on injection	12	1
Spontaneous movement	2	0
Hiccough	0	4
Average peak decrease in systolic pressure (%)	31	22.5
Incidence of > 30% decrease in arterial pressure	19	9

least increase and had the lowest IOP after intubation. The IOP decreased over the 2 minutes after intubation and was significantly below the baseline levels in all groups (p < 0.05 to p < 0.001). The IOP in both the propofol groups was significantly lower (p < 0.01) than in the two thiopentone groups, with the lowest IOP in the group that received the additional dose of propofol.

Systolic arterial pressures and heart rates are given in Tables 3 and 4. There was a significant decrease (p < 0.05 to p < 0.001) in systolic arterial pressure in the two propofol groups throughout the period of study, with a peak average decrease of just under 30% observed just before intubation. There was no greater decrease in arterial pressure in the group that received the supplementary dose of propofol. Arterial pressure decreased significantly (p < 0.01) in the thiopentone groups as well as on induction of anaesthesia (peak decrease of approximately 20%) but it increased to near baseline values with intubation and was not significantly different from the baseline values from then on except for a significant decrease (p < 0.05) at 2 minutes after intubation in the group that received the supplementary dose. The difference between the propofol and thiopentone groups was significant from the time of intubation onwards. Heart rate changes were generally small in magnitude; the propofol groups showed a slight decrease and the thiopentone groups an increase, which was significant (p < 0.05) after intubation.

The incidence of side effects (Table 5) was generally low, apart from the greater incidence of pain on injection and greater incidence and severity of hypotension with propofol. Nineteen out of 40 patients given propofol showed a greater than 30% decrease in systolic arterial pressure; eight of these were in the supplementary dose group. In contrast,

only nine patients who received thiopentone had such a decrease in arterial pressure. The decrease in arterial pressure was either short-lasting or responded to intravenous infusion of 500–1000 ml crystalloid solutions. The overall quality of induction was graded as good in 34 and adequate in six patients with each of the two induction agents. Emetic sequelae were observed in eight patients each in the propofol and thiopentone groups in the immediate postoperative period.

Discussion

It is well known that the stimulus of intubation is associated with an increase in IOP.^{7–9} This increase disappears in a few minutes and may not be of any great consequence in the majority of patients who undergo elective ophthalmic surgery but it may be harmful to many patients with compromised retinal circulation or patients with poorly perfused optic discs and elevated IOP. The present study shows the importance of the induction agent and the relaxant used to facilitate tracheal intubation. It is clear that propofol is associated with somewhat better control of IOP, as shown previously.^{5,6} The present study shows that intubation facilitated with vecuronium, even when thiopentone is used for induction, is associated with IOPs which are lower than baseline values, in contrast to the significant elevations observed when suxamethonium is used.⁶ This is possibly due to an IOP lowering effect of vecuronium itself.^{10,11}

The advantage of a smaller supplementary dose of the induction agent is clear in the present study; IOPs after intubation in these groups were lower than in the corresponding single dose groups. Propofol is clearly more effective than thiopentone in this respect, and IOPs subsequent to intubation were also lowest in this group. Similar attenuation of the increase in IOP with a supplementary dose of propofol was also reported where suxamethonium was used to facilitate intubation.⁶ The better control of IOP with propofol may be due to a greater decrease in arterial pressure associated with its use^{2,5,12} to the lack of any ant-analgesic effect¹³ or to a greater depth of anaesthesia.¹⁴

Factors such as central venous pressure and arterial carbon dioxide tension may influence the IOP in addition to arterial pressure and the depth of anaesthesia. Central venous pressure was not measured in the present study since

it was considered unnecessary on ethical grounds but all patients were kept horizontal throughout the period of study. Ventilation was assisted throughout to prevent accumulation of carbon dioxide. Moreover, changes in these parameters would affect all the groups in a similar fashion.

Hypotension occurred more frequently with propofol and arterial pressure decreased to a greater extent. This is a drawback and requires care, particularly in the elderly. However, the hypotension responds readily to infusion of crystalloid solutions and its severity may be lessened by a reduction in dosage, particularly in elderly patients. Pain on injection is the only other significant disadvantage of propofol but this may also be reduced if the drug is injected into larger veins in the forearm or antecubital fossa,³ or by administration in a mixture with lignocaine.¹⁵

In conclusion, the use of propofol and vecuronium for induction of anaesthesia and tracheal intubation respectively is associated with better control of IOP than a thiopentone-vecuronium sequence. The administration of a second, smaller dose of both induction agents results in further attenuation of the increase in IOP associated with tracheal intubation and propofol produces a significantly better effect.

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References

- CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA, STEPHENSON DK. Dose requirements of ICI 35868 (Propofol, 'Diprivan' in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1168-71.
- MACKENZIE N, GRANT IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *British Journal of Anaesthesia* 1985; **57**: 725-31.
- MCCOLLUM JSC, DUNDEE JW. Comparison of the induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41**: 995-1000.
- EDELST G. A comparison of propofol and thiopentone as induction agents in outpatient surgery. *Canadian Journal of Anaesthesia* 1987; **34**: 110-6.
- MIRAKHUR RK, SHEPHERD WFI. Intraocular pressure changes with propofol ('Diprivan'): comparison with thiopentone. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 41-4.
- MIRAKHUR RK, SHEPHERD WFI, DARRAH WC. Propofol or thiopentone: effects on intraocular pressure associated with induction of anaesthesia and tracheal intubation (facilitated with suxamethonium). *British Journal of Anaesthesia* 1987; **59**: 431-6.
- GOLDSMITH E. An evaluation of succinylcholine and gallamine as muscle relaxants in relation to intraocular tension. *Anesthesia and Analgesia* 1967; **46**: 557-61.
- PANDEY K, BADOLA P, KUMAR S. Time course of intraocular hypertension produced by suxamethonium. *British Journal of Anaesthesia* 1972; **44**: 191-6.
- JOSHI C, BRUCE DL. Thiopental and succinylcholine action on intraocular pressure. *Anesthesia and Analgesia* 1975; **54**: 471-5.
- JANTZEN J-P, HACKETT GH, ERDMANN K, EARNSHAW G. Effect of vecuronium on intraocular pressure. *British Journal of Anaesthesia* 1986; **58**: 433-6.
- MIRAKHUR RK, SHEPHERD WFI, LAVERY GG, ELLIOTT P. The effects of vecuronium on intra-ocular pressure. *Anaesthesia* 1987; **42**: (in press).
- FAHY LT, VANMOURIK GA, UTTING JE. A comparison of the induction characteristics of thiopentone and propofol (2,6-diisopropylphenol). *Anaesthesia* 1985; **40**: 939-44.
- BRIGGS LP, DUNDEE JW, BAHAR M, CLARKE RSJ. Comparison of the effect of diisopropyl phenol (ICI 35868) and thiopentone on response to somatic pain. *British Journal of Anaesthesia* 1982; **54**: 307-11.
- DOZE VA, WESTPHAL LM, WHITE PF. Comparison of propofol with methohexital for outpatient anaesthesia. *Anesthesia and Analgesia* 1986; **65**: 1189-95.
- BROOKER J, HULL CJ, STAFFORD M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40**: 91-2.

Changes in intra-ocular pressure in the elderly during anaesthesia with propofol

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J. P. EGRETEAU

Summary

Variations in intra-ocular pressure during anaesthesia were studied in two groups of 15 elderly patients selected randomly. The groups were not significantly different with regard to age, sex, weight or ASA classification. The first group received intravenous propofol as a bolus followed by a continuous infusion. The second group received a bolus of thiopentone followed by maintenance with enflurane. Intra-ocular pressure, heart rate and arterial pressure were measured before and after induction, after intubation and at the end of the operation. Overall, compared with baseline values, the results showed a decrease in intra-ocular pressure of 31% in group 1 and 17% in group 2, and a decrease in systolic arterial pressure of 14% in both groups.

Key words

Anaesthesia, geriatric.

Measurement techniques; intra-ocular pressure.

Propofol is a non-barbiturate intravenous anaesthetic agent which allows rapid induction of anaesthesia and early recovery. It may be suitable for use in elderly patients who undergo ophthalmic surgery.

The aim of this study was to compare intra-ocular pressure (IOP), systolic and diastolic arterial pressures and heart rate in two groups of patients, one of which received a bolus dose of propofol followed by continuous infusion and the other a bolus dose of thiopentone followed by maintenance with enflurane.

Patients and methods

The study was carried out in 30 patients (14 male) classed as ASA grade 2 or 3, with no hepatic or renal dysfunction and no history of allergy. They were scheduled for ophthalmic surgery under general anaesthesia and were randomly allocated to receive either propofol or thiopentone and enflurane. Patients were given intramuscular premedication with flunitrazepam 0.75 mg and atropine 0.5–1.0 mg according to weight, one hour before induction of anaesthesia.

Patients in group 1 received a mean bolus dose of propofol of 1.8 mg/kg (SEM 0.1) followed by a continuous infusion at a mean rate of 5.2 mg/kg/hour (SEM 0.4) until the end of the operation. The patients' tracheas were intubated after administration of vecuronium and their lungs

ventilated with 50% oxygen–nitrous oxide. Fentanyl was administered at the onset of surgery. Anaesthesia in group 2 was induced with thiopentone 6.8 mg/kg (SEM 0.3). Intubation and ventilation were carried out in the same way as in group 1. Anaesthesia was maintained with enflurane 1.1% (SEM 0.1%).

Intra-ocular pressure was measured in both eyes before premedication, before and after induction and before and after intubation; and at the end of surgery, before withdrawal of the anaesthetic agents, in the eye not operated upon. The measurements were recorded by the surgeon with a hand-held applanation tonometer (Perkins).

Systolic and diastolic arterial pressures and heart rate were recorded continuously using a Dinamap machine. Only those values which corresponded to the times of measurement of IOP were taken into account. The duration of anaesthesia was recorded and the time between the end of anaesthesia and extubation.

Statistical analysis was assessed on a pre-programmed IBM PC AT and Student's *t*-test, the Chi-squared test and analysis of variance were carried out.

Results

The patient groups were comparable with regard to sex, age, weight, ASA index, IOP and heart rate before surgery

Table 1. General patient characteristics. Values expressed as mean (SEM) or number of patients, as appropriate.

	Group 1 (propofol)	Group 2 (thiopentone–enflurane)
Sex, M/F	10/5	6/9
Age, years	73.6 (2.1)	71.6 (0.2)
Weight, kg	60.3 (2.8)	65.6 (3.1)
ASA grade 2/grade 3	7/8	8/7
IOP, mmHg		
Before premedication	16.6 (1.3)	17.0 (1.08)
After premedication	18.0 (1.2)	17.0 (1.5)
Systolic blood pressure, mmHg	145.9 (7.4)	147.3 (5.7)
Diastolic blood pressure, mmHg	86.9 (4.1)	88.4 (2.3)
Heart rate, beats/minute	72.0 (4.0)	73.0 (2.0)
Duration of anaesthesia, minutes	68.0 (7.4)	82.3 (12.9)
Time between end of anaesthesia and extubation, minutes	38.0 (5.5)	26.8 (4.5)

No significant differences between groups.

(Table 1). No significant difference was found between IOP measured on each eye but only the IOP of the unoperated eye has been included in the study. The different types of surgery performed on the patients in both groups are listed in Table 2.

Table 2. Types of surgery in each group of patients.

	Group 1 (propofol)	Group 2 (thiopentone–enflurane)
Cataract extraction	12	7
Strabismus	1	—
Dacryocystectomy	1	—
Secondary implantation	1	—
Detachment of the retina	—	3
Vitrectomy	—	2
Trabeculectomy	—	3

There was no significant difference between the IOPs of the two groups during anaesthesia (Table 3). IOP in group 1 decreased by 31% ($p < 0.001$) from the baseline value and 17% in group 2 ($p < 0.05$). The measurement after administration of vecuronium and intubation was not significantly different from that after induction but was significantly different from baseline in both groups.

Table 3. Mean (SEM) IOP in each group, mmHg.

	Group 1 (propofol)	Group 2 (thiopentone–enflurane)
Before induction	18.0 (1.2)	17.0 (1.5)
After induction	12.6 (1.1)***	14.4 (1.8)*
After intubation	13.7 (1.2)***	14.8 (1.7)**
After surgery	10.7 (1.0)***	13.0 (1.3)***
Mean after induction	12.3 (1.1)***	14.0 (1.5)**

No significant difference between groups. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, significant changes from baseline.

There was no significant difference in arterial pressure between the groups (Table 4). The mean decrease in systolic arterial pressure of 14% was significant in both groups ($p < 0.001$). The mean decrease in diastolic arterial pressure was 9.7% in group 1 and 9.3% in group 2. This difference was significant ($p < 0.01$) when compared with

Table 4. Mean (SEM) systolic and diastolic blood pressures, mmHg.

	Group 1 (propofol)	Group 2 (thiopentone–enflurane)
Systolic blood pressure		
Before induction	145.9 (7.4)	147.3 (5.7)
After induction	119.5 (5.8)***	131.9 (5.3)**
After intubation	140.7 (6.2)	137.1 (7.2)
After surgery	115.7 (5.0)***	114.6 (5.8)***
Mean after induction	125.0 (5.6)***	127.8 (6.1)***
Diastolic blood pressure		
Before induction	86.9 (4.1)	88.4 (2.3)
After induction	76.5 (3.5)**	81.9 (2.2)**
After intubation	83.9 (3.4)	84.0 (2.4)
After surgery	74.8 (3.3)***	74.5 (3.7)***
Mean after induction	78.4 (3.4)**	80.1 (2.6)**

No significant difference between groups. ** $p < 0.01$, *** $p < 0.001$, significant changes from baseline.

baseline values. However, diastolic and systolic pressures after intubation were not significantly different from baseline values. A decrease in heart rate of 17% ($p < 0.001$) was noted in both groups at the end of surgery (Table 5). The interval between the end of anaesthesia and extubation did not differ significantly between the groups (Table 1).

Table 5. Mean (SEM) heart rate, beats/minute.

	Group 1 (propofol)	Group 2 (thiopentone–enflurane)
Before induction	72 (3.9)	73 (2.5)
After induction	74 (2.8)	79 (3.0)
After intubation	72 (3.6)	82 (3.3)
After surgery	60 (2.8)***	65 (2.8)***

No significant difference between groups. *** $p < 0.001$, significant changes from baseline.

Discussion

Elderly patients who undergo lengthy ophthalmic surgery under general anaesthesia require a stable induction with little haemodynamic depression in order to maintain ocular immobility and a decrease of IOP.¹ Short anaesthesia without coughing or vomiting favours rapid recovery and avoids ocular complications.

Thiopentone, enflurane and fentanyl cause a decrease in IOP during anaesthesia.^{2,3} Propofol produces a large decrease in IOP which can be greater than that observed with thiopentone or enflurane.^{4–6} We also found no change in IOP after intubation under vecuronium, in agreement with previous reports.⁷

In conclusion, propofol can be used as effectively as thiopentone and enflurane for general anaesthesia in elderly patients who undergo ophthalmic surgery. It has notable effects on intra-ocular pressure.

References

- ADAMS AK, JONES RM. Anaesthesia for eye surgery: general considerations. *British Journal of Anaesthesia* 1980; **52**: 663–9.
- RUNCIMAN JC, BOWEN-WRIGHT RM, WELSH NH, DOWNING JW. Intraocular pressure changes during halothane and enflurane anaesthesia. *British Journal of Anaesthesia* 1978; **50**: 371–5.
- FENECK RO, DURKIN MA. A comparison between the effects of fentanyl, droperidol with fentanyl and halothane anaesthesia on intra-ocular pressure in adults. *Anaesthesia* 1987; **42**: 266–9.
- BARALE F, HAGOPIAN F, FRANÇOIS P, GIROD A, BACHOUR K, SERRI S, STIMMESSE B, ROYER J. Utilisation du propofol en

- anesthésie ophtalmologique chez le vieillard. *Annales Françaises d'Anaesthésie et Réanimation* 1987; **6**: 309–12.
5. MIRAKHUR RK, SHEPHERD WFI. Intraocular pressure changes with propofol ('Diprivan'): comparison with thiopentone. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 41–4.
6. LEVEQUE M, RAKOTOSEHENO JC, MIMOUNI F, ROUFFY P, EGRETEAU JP. Effets du propofol sur la pression intraoculaire au cours de l'induction anesthésique. *Annales Françaises d'Anaesthésie et Réanimation* 1987; **6**: 306–9.
7. SIA RL, RASHKOVSKY OM. Org NC 45 and intraocular pressure during anaesthesia. *Acta Anaesthesiologica Scandinavica* 1981; **25**: 219–21.

Propofol for electroconvulsive therapy

A comparison with methohexitone. Preliminary report

E. C. ROUSE

Summary

Twenty patients who received electroconvulsive therapy were anaesthetised with either propofol or methohexitone in a randomised crossover study. Recovery times were similar but patients who received propofol tended to be orientated sooner. The decrease in arterial blood pressure after induction was greater with propofol than with methohexitone. There was an increase in blood pressure immediately after therapy in patients who received methohexitone but not in those given propofol. There was a slight difference in pain on injection. The mean duration of convulsion (measured in 10 patients) during anaesthesia was shorter with propofol than with methohexitone.

Key words

Anaesthesia; electroconvulsive therapy
Anaesthetics, intravenous; methohexitone, propofol.

Patients who present for electroconvulsive therapy (ECT) are usually of ASA grade 1 or 2 and most suffer from severe depressive illnesses. ECT is usually given twice weekly for a minimum of six treatments, so it is important that the anaesthetic should be very acceptable. It should produce a deep level of anaesthesia quickly with a rapid recovery and minimal side effects, and it has to be compatible with the wide range of drugs that these patients receive. Propofol has been shown to improve the speed and quality of recovery¹ and animal studies show no marked interaction between propofol and tricyclic antidepressants or monoamine oxidase inhibitors.²

This study was set up to compare the anaesthetic and recovery profile of propofol with that of methohexitone, which is one of the more commonly used agents for anaesthesia for ECT. The trial was approved by the hospital ethical committee and verbal informed consent was obtained from patients. This report considers data from the first 20 patients in a trial in which 40 patients are to be included.

Methods

So far 20 patients (18 female) of ASA grade 1 or 2, aged between 19 and 73 years (mean 51.1, SD 15.8), have been entered into the trial. Their weights ranged from 42-74 kg (mean 57.7, SD 8.53). They were receiving treatment with a wide variety of agents (Table 1) and tended to receive large doses of drugs at night. ECT was always done in the mornings.

Table 1. Psycho-active and other therapy received by patients.

Psycho-active	Others
Amitriptyline	Aminophylline slow
Carbamazepine	Amiloride
Chlorodiazepoxide	Bendroflumazide
Chloral mixture	Lactulose
Chlorpromazine	Menophase
Diazepam	Ranitidine
Dothiepin	Tamoxifen
Flupenthixol decanoate	
Haloperidol	
Imipramine	
Isocarboxazid	
Lofepamine	
Mianserin	
Nitrazepam	
Oxazepam	
Perphenazine	
Temazepam	
Thioridazine	
Triazolam	
Trifluoperazine	
Trimipramine	
Tryptophan	

Patients were anaesthetised on four occasions so that they received propofol twice and methohexitone twice in a paired crossover manner. The first and third treatments were allocated randomly to either propofol or methohexitone; the other drug was given on the second and fourth occasions. One patient was withdrawn after only two anaesthetics because she developed hypomania.

Each patient was premedicated with promethazine 25 mg

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Table 2. Effects of propofol and methohexitone on diastolic and systolic arterial pressures. Values expressed as mean (SD).

	Propofol		Methohexitone	
	Systolic, mmHg	Diastolic, mmHg	Systolic, mmHg	Diastolic, mmHg
Baseline	141.8 (18.8)	81.0 (12.7)	141.8 (18.8)	81.0 (12.7)
Induction	124.0 (14.0)	75.0 (14.2)	133.5 (18.6)	85.8 (12.8)
After ECT	138.8 (26.4)	82.0 (14.9)	157.3 (29.3)	93.2 (13.6)
Mean to sit	121.7 (18.4)	69.0 (10.5)	133.8 (18.2)	76.5 (9.9)
On sitting	118.5 (15.0)	65.0 (7.8)*	129.3 (16.9)	73.3 (12.3)
On standing	111.0 (23.7)	69.0 (13.1)†	121.3 (25.7)‡	74.5 (19.6)

* n = 33; † n = 27; ‡ n = 25.
Number of administrations of each agent was 38 unless specified otherwise.

intramuscularly approximately one hour before anaesthesia. An initial dose of atropine 0.3 mg was given intravenously followed by the anaesthetic agent. This was titrated at the rate of 2 ml every 5 seconds for propofol or 1 ml every 5 seconds for methohexitone. The injection was stopped when the observer (E.C.R.) judged the patient to be anaesthetised with loss of the eyelash reflex as a guide, and the time noted. A minimum dose of suxamethonium 25 mg completed the anaesthetic. One hundred percent oxygen was administered until the suxamethonium took effect.

The same observer gave the anaesthetic and made the initial observations each time. A vein on the dorsum of the hand was used whenever possible, both to allow the three drugs to be given through a butterfly needle and because this is safer than use of the antecubital fossa. Some depressed patients are more inclined to move during injection than are patients who present for surgery. Each patient received the same dose of each agent on subsequent occasions. Any verbal or facial indication of pain during induction was noted but no leading questions were asked about this.

A bilateral electroconvulsive shock was given using a constant current ECTRON Duopulse machine (ECT2, 233.75 millicoulombs for 4 seconds). The length of the resulting convulsion from the time of the shock to the last twitch of the clonic phase, was recorded in 10 patients by another observer (G.P.) with a stopwatch. Patients' lungs were ventilated with oxygen by facemask until spontaneous respiration returned. They were then turned onto their left side.

Arterial blood pressure was recorded before and immediately after the injection of the anaesthetic and then every 2 minutes until the patient was able to stand. Recordings were made with a Critikon Dinamap. ECT was administered just after the first recording of blood pressure following induction.

Assessment of recovery

The same two observers (E.C.R. and G.P.) assessed the patients during the recovery phase. It was not possible to use complex tests because the confusion that follows ECT is very similar to the postictal phase of a grand mal convulsion. The patients' previous mental state and the drugs they have received can also add to their confusion.

The four criteria were therefore deliberately kept simple. They were the times from induction until the patient was able to open eyes on command, to answer the question 'Where are you?', to sit up and to stand.

Results

The mean doses of propofol and methohexitone were 2.0 mg/kg (SD 0.4) and 1.4 mg/kg (SD 0.3), respectively. The arterial blood pressures are presented in Table 2. Propofol depressed arterial blood pressure on induction to a greater extent than methohexitone. An increase in blood pressure was sometimes seen in patients immediately after ECT but there was then usually a rapid decrease over a period of about 2 minutes. The increase was seen in patients who received methohexitone but not in those who had propofol. One woman with a history of angina and alcoholism who weighed 62 kg, had a mean initial arterial pressure of 176/97 mmHg which increased to 219/124 mmHg after methohexitone 130 mg. Her highest level after propofol 160 mg was 156/92 mmHg. The blood pressure during the rest of the recovery period remained lower after propofol than after methohexitone.

Recovery times are listed in Table 3. The time to open

Table 3. Recovery times after anaesthesia with propofol or methohexitone. Values expressed as mean (SD).

Time in minutes until:	Propofol	Methohexitone
Eyes open	8.7 (2.2)	8.2 (2.0)
Able to sit	17.1 (3.9)	16.8 (4.5)
Oriented	19.6 (6.0)	21.7 (10.2)
Able to stand	24.9 (5.6)	24.3 (5.6)

Number of administrations of each agent was 38.

eyes was similar after each agent, as were the times to sit and to stand. Orientation tended to return a little more quickly with propofol.

Mood was assessed before the patient stood, as not distressed, distressed or very distressed. The mood of most patients seemed to be very similar to that prior to ECT after both drugs. A few were distressed and crying (Table 4); none was euphoric. The incidence of pain on injection was low in both groups but propofol caused twice as many complaints as methohexitone (Table 4).

The duration of convulsion was timed from the start of the electrical impulse to the last of the clonic contractions

Table 4. Pain on injection and mood changes observed for propofol and methohexitone.

	Propofol	Methohexitone
Number of administrations	38	38
Pain on injection	8	4
Mood change	5	1

Number of administrations of each agent was 38.

in 10 patients. No apparent difference in the size or range of seizure was noted between the two drugs but the mean duration of convulsion during anaesthesia was shorter with propofol than with methohexitone (Table 5). The dose of suxamethonium was kept constant for each patient in each of the four anaesthetics.

Table 5. Duration of seizure in seconds during anaesthesia with propofol or methohexitone.

Patient	Propofol	Methohexitone
1	17.5	23.1
2	16.1	24.2
3	16.5	19.3
4	16.8	44.6
5	23.4	44.2
6	18.4	23.0
7	18.3	43.5
8	16.5	29.8
9	13.9	27.7
10	22.5	29.0
Mean (SD)	18.0 (2.8)	30.8 (9.2)

Number of administrations of each agent was 20.

Discussion

It is widely believed that convulsive activity in the brain is crucial to the therapeutic efficacy of ECT.^{3,4} Until recently ECT was not considered to have been administered successfully unless the tonic convulsion was followed by a series of clonic convulsions. Some recent work on the electrical currents passed has caused doubt as to whether the length and type of seizure are of any consequence.⁵⁻⁸ No patient in this trial failed to have a tonic convulsion followed by the clonic phase, although the latter was considerably shorter after propofol than after methohexitone. Further analysis of this finding which takes into account the patients' other medication, still has to be done. The analysis will also have to consider the increase in seizure threshold as treatment progresses.⁹

Animal studies of propofol have shown neither convulsant nor anticonvulsant action. Most barbiturates have anticonvulsant effects² but methohexitone can cause central nervous excitation which is seen as muscular twitching. It is therefore not regarded as a suitable anaesthetic for epileptic patients, although such patients rarely present for ECT. The Committee on Safety of Medicines recently reported nine cases of convulsions or involuntary movements that occurred in epileptics and non-epileptics during induction of, or emergence from anaesthesia induced by propofol. It is therefore interesting that this study shows a reduced seizure length in patients anaesthetised with propofol compared with those who received methohexitone. The difference between the two drugs may be due in part to the excitatory effect of methohexitone but it may also indicate some anticonvulsant action of propofol. There was no difference in the size and range of the movements during the seizure so it is unlikely that any muscle relaxant action is involved.

The mental state of the patients, some of the drugs they receive and especially the effect of the marked postictal phase of ECT, preclude any complex assessment of recovery after anaesthesia. There is little difference in the immediate recovery profile of the two drugs. Further assessments of orientation need to be made later in the recovery phase. A few more patients cried after propofol than after methohexitone but this lasted for only a few

minutes in each case and was not considered to be clinically significant.

A contraindication to ECT is an elevated intracranial pressure, since it is known that ECT can increase the arterial blood pressure. The increase in this study was more marked in some patients than in others but it was not predictable from the baseline blood pressure. It has been claimed that the temporary impairment of cognitive function associated with ECT correlates highly with the magnitude of the associated increase in arterial pressure¹⁰ and it may be preventable by drugs which abolish or reduce this increase. Propofol appears to effect such a reduction and may therefore have some clinical value.

The incidence of pain assessed as severe because it was expressed spontaneously, was 21% for propofol compared with 10.5% for methohexitone. The use of lignocaine to minimise pain on injection was avoided, since lignocaine attenuates ECT-induced seizures. It has been reported that the antidepressant effect of ECT is reduced when seizures are shortened by lignocaine.¹¹

In conclusion propofol may have a use in ECT because it reduces the increase in arterial blood pressure after seizure but further work is needed to determine whether the reduction of seizure length has any effect on the therapeutic efficacy of ECT.

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References

- O'TOOLE DP, MILLIGAN KR, HOWE JP, MCCOLLUM JSC. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia. *Anaesthesia* 1987; **42**: 373-6.
- GLEN JB, HUNTER SC, BLACKBURN TP, WOOD P. Interaction studies and other investigations of the pharmacology of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 7-14.
- KENDELL RE. Review article. The present status of electroconvulsive therapy. *British Journal of Psychiatry* 1981; **139**: 265-83.
- OTTOSSON J-O. Use and misuse of electroconvulsive treatment. *Biological Psychiatry* 1985; **20**: 933-46.
- ROBIN A, DE TISSERA S. A double-blind controlled comparison of the therapeutic effects of low and high energy electroconvulsive therapies. *British Journal of Psychiatry* 1982; **141**: 357-66.
- DEAKIN JFW. Antidepressant effects of electroconvulsive therapy: current or seizure? *British Medical Journal* 1983; **286**: 1083-4.
- RICH CL, BLACK NA. The efficiency of ECT. II. Correlation of specific treatment variables to response rate in unilateral ECT. *Psychiatry Research* 1985; **16**: 147-54.
- PRICE TRP, MCALLISTER TW. Response of depressed patients to sequential unilateral nondominant brief-pulse and bilateral sinusoidal ECT. *Journal of Clinical Psychiatry* 1986; **47**: 182-6.
- SACKHEIM H, DECINA P, PROHOVNIK I, MALITZ, S. Seizure threshold in electroconvulsive therapy. Effects of sex, age, electrode placement and number of treatments *Archives of General Psychiatry* 1987; **44**: 355-60.
- HAMILTON M, STOCKER MJ, SPENCER CM. Post-ECT cognitive

defect and elevation of blood pressure. *British Journal of Psychiatry* 1979; **135**: 77-8.

11. CRONHOLM B, OTTOSSON J-O. Experimental studies of the therapeutic action of electroconvulsive therapy in endogenous

depression. The role of the electrical stimulation and of the seizure studied by variation of stimulus intensity and modification by lidocaine of seizure discharge. *Acta Psychiatrica Scandinavica* 1960; **35** (Suppl. 143): 69-102.

Propofol and emesis

R. D. GUNAWARDENE AND D. C. WHITE

Summary

Ninety patients scheduled to undergo minor gynaecological surgery were divided into three groups. Group 1 received propofol only, for both induction and maintenance of anaesthesia. Group 2 were given propofol for induction and maintenance but inhaled 66% nitrous oxide in addition. Group 3 had propofol for induction only and were given nitrous oxide and enflurane thereafter. The incidence of nausea in group 1 was 0%, in group 2, 3.4% and in group 3, 9.4%. No patient vomited.

Key words

Anaesthetics, intravenous; propofol.

Complications; nausea, vomiting.

Nausea and vomiting remain a problem in the post-operative period. The objective of the present study was to determine the incidence of nausea and vomiting when propofol was used alone or in combination with other agents to produce anaesthesia for minor gynaecological procedures in elective day care and short stay patients.

Methods

Seventy-eight patients and 12 short stay patients admitted for minor gynaecological operations were included in the study. Day care patients received no premedication; short stay patients were given temazepam 10 mg orally 2 hours pre-operatively. All patients studied were of ASA grade 1 or 2 and in the age range 22–67 years. They were visited by the anaesthetist a few hours before surgery. The objective of the study and the anaesthetic techniques were explained to them and their consent obtained. No patient with a history of drug allergy was included.

Patients were allocated randomly to one of three groups to receive either propofol and air (group 1), propofol, nitrous oxide 66% and oxygen 33% (group 2) or propofol, nitrous oxide 66%, oxygen 33% and enflurane 2–3% (group 3).

A 23-gauge indwelling needle was inserted into a vein on the dorsum of the hand on arrival in the anaesthetic room. Arterial blood pressure and pulse rate were recorded before induction of anaesthesia. Lignocaine 1%, 1–2 ml was mixed with propofol 20 ml in the syringe and the mixture injected until loss of the eyelash reflex. Induction time was similar

to that after thiopentone, i.e. less than one minute.¹ The quality of induction was good as found by others.^{2,3} Group 2 patients were then given 66% nitrous oxide and oxygen; group 3 patients were given the same with added enflurane sufficient to prevent movement.

A further 10 mg propofol was given intravenously once the patients were transferred to the operating table before they were positioned. Incremental doses of propofol 20–30 mg were given to maintain surgical anaesthesia in groups 1 and 2. Pulse rate and arterial blood pressure recordings were made at 5–10-minute intervals. Rapid lightening of anaesthesia during surgery was noted in group 1 patients but after a little practice it was found easy to anticipate the surgical stimulus.

Administration of nitrous oxide or nitrous oxide and enflurane was discontinued at the completion of surgery, which was after about 5–10 minutes. All patients were placed in the left lateral position after transfer to a trolley and then taken to the recovery area. The nurse in charge of the patient was asked to record any nausea or vomiting and any medication administered in the recovery room and in the postoperative period up to the time of discharge.

All the patients were visited postoperatively by the anaesthetist and questioned about nausea and vomiting since they had regained consciousness.

Results

Details of the three groups of patients and the total doses of propofol are given in Table 1. Induction of anaesthesia

Table 1. Details of patients.

	Group 1 (n = 29)	Group 2 (n = 29)	Group 3 (n = 32)
Mean age (years)	42.55	43.48	40.15
Mean weight (kg)	60.27	67.75	64.24
Mean dose of propofol (mg)	280.37	260.37	134.63

with propofol was uneventful; dosages of approximately 2 mg/kg were used. Two patients had to be excluded from the study because of bouts of coughing and inability to achieve surgical anaesthesia with propofol, nitrous oxide and oxygen. They eventually settled with thiopentone, nitrous oxide, oxygen and halothane. Both weighed over 100 kg and were heavy smokers. No venous phlebitis or allergic response to propofol was seen. A few patients received an induction dose of propofol of 3 mg/kg and were noted to have respiratory depression of short duration (1–2 minutes) after induction of anaesthesia, and transient hypotension; the arterial pressure decreased by 20–30 mmHg.

The incidence of nausea and vomiting is shown in Table 2,

Table 2. Incidence of nausea and vomiting.

	Group 1 (n = 29)	Group 2 (n = 29)	Group 3 (n = 32)	Groups 1, 2 & 3 (n = 90)
Number of patients with past history of nausea and vomiting	5	6	3	14
Number of patients who felt nauseated postoperatively in this study	0 (0%)	1 (3.4%)	3 (9.4%)	4 (4.44%)
Exact 95% confidence limits (Documenta Geigy)	0–12	0.1–18	2–25	1.2–11

which also gives the number of patients in each group who gave a history of nausea and/or vomiting after previous anaesthetics. No vomiting was recorded in any of the patients studied; 14 patients (15.4%) gave a history of vomiting related to general anaesthesia in the past.

One of the disadvantages of propofol is the occurrence of involuntary movements of the hands and arms. An incidence of 2.2% of such movements was seen in patients of groups 1 and 2, but none in group 3. These movements were slight and transient and were not a problem in clinical practice. Pain on injection was seen in five patients (5.5%) along the arm, and three patients (3.3%) in group 1 and group 2 experienced headache in the postoperative period but only one needed analgesics. Addition of 1 ml lignocaine 1% to the syringe before injection of propofol appears to reduce the incidence of pain on injection.

The overall incidence of nausea in all the patients studied was 4.4% (four patients); the nausea lasted for 5–15 minutes. No medication was administered and the symptoms disappeared spontaneously. These patients were free from nausea or emesis until discharge up to 24 hours postoperatively. Three patients received syntocinon 5 units intravenously but none was nauseated postoperatively. The quality of recovery was good and free from hallucinations,

tremors or restlessness, and patients were clear-headed and comfortable.

Discussion

The overall incidence of nausea and vomiting after anaesthesia has been studied extensively. Table 3 is taken from a comprehensive review of the subject by Palazzo and Strunin⁴ and gives figures from many studies. The overall incidence of emetic sequelae lies between 20 and 40%. These authors confirm the generally held view that nausea and vomiting is between two and three times as frequent in female as in male patients. It has been suggested that the cause of this is hormonal.⁵ The figures given in Table 3

Table 3. Selected studies on the incidence of emetic sequelae following anaesthesia.⁴

Investigator	Population size	Incidence (%)	Follow-up (hours)	NVR*	Year
Waters, R.M.	10 000	40.6	NA	NV	1936
Dent, S.	3000†	27.2	24	VR	1955
Burtles & Peckett	1701†	32.0	24–36	NV	1957
Bonica, J.	1561†	30.5	24	NVR	1958
Bellville, J.W.	748†	19.4	25	NV	1959
Adriani, J.	2230†	23.0	mean 6	RV	1961
McKie, B.D.	110†‡	30.9	24	NV	1969
Korttila, K.	40†‡	55.0	24	NVR	1979
Mortensen, P.T.	96†‡	34.4	24	NVR	1982

* Nausea; V, vomiting; R, retching.
NA, Not available; † prospective study; ‡ females only.

refer to patients of both sexes and it was found that the incidence of nausea and vomiting after minor gynaecological surgery is between 20 and 40%. A recent study⁶ found an incidence of nausea and vomiting of 47% in minor gynaecological day patients. All the patients in this series received both fentanyl and etomidate during the anaesthetic. It was also suggested by Dundee *et al.*⁷ that a greater incidence of emetic sequelae occurs after cervical dilatation as compared to uterine curettage without preliminary dilatation of cervix, as in incomplete abortion.

Of great interest is the relationship between postoperative emetic sequelae and the anaesthetic agent used. A comprehensive study on this subject was carried out in Belfast⁸ and Table 4, taken from this work, shows the considerable difference in incidence of both nausea and vomiting attributable to different anaesthetic agents. The incidence of emesis after isoflurane anaesthesia⁴ is comparable to that after other inhalational agents.

The results of our study are outstandingly good in the light of the existing literature on this subject, and confirm the findings in Table 4. It has been suggested that nitrous

Table 4. Percentage frequency of nausea and vomiting during the first 6 hours after minor gynaecological surgery with atropine premedication and intermittent intravenous, nitrous oxide–oxygen anaesthesia.⁸

Main anaesthetic	Vomiting	Nausea	Nil
Thiopentone 4 mg/kg	11	6	83
Methohexitone 1.6 mg/kg	14	12	74
Propanidid 4 mg/kg	25	18	57
Diazepam 0.6–0.8 mg/kg	5	3	92
Althesin 50 µl/kg	5	7	88
Ketamine 1.0–3.0 mg/kg	18	23	59
Etomidate 0.3 mg/kg	27	12	61
Propofol 2.0 mg/kg	0	5	95

oxide causes emetic symptoms,⁹ although this is not confirmed in a more recent study from the Mayo Clinic.¹⁰ Our results do not show any emetic effect attributable to nitrous oxide.

Oxygen saturation was monitored by pulse oximeter in 10 patients of group 1 who underwent dilatation and curettage and were anaesthetised with propofol alone. Saturation remained above 90% in all patients.

Intermittent administration of intravenous propofol as the sole agent produced a fluctuating level of anaesthesia with consequent surgical inconvenience. We found with practice that this could be almost eliminated but better results could, no doubt, be obtained by continuous infusion of propofol. Infusion rates in the region of 10 mg/kg/hour (breathing air) or 9 mg/kg/hour with nitrous oxide have been found to be satisfactory by various workers.^{11,12}

The routine use of propofol as the main agent for anaesthesia appears almost to eliminate nausea and vomiting as a postoperative complication of minor gynaecological surgery. It is reasonable to assume that this will apply to other forms of surgery in which the use of opioids and other causes of emesis, such as abdominal trauma, are not involved.

References

1. BRIGGS LP, CLARKE RSJ, DUNDEE JW, MOORE J, BAHAR M, WRIGHT PJ. Use of di-isopropyl phenol as main agent for short procedures. *British Journal of Anaesthesia* 1981; **53**: 1197-1202.
2. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, SEAR JW, SPENCE AA, STEPHENSON DK. Dose requirements of ICI 35868 (propofol-Diprivan) in a new formulation for induction for anaesthesia. *Anaesthesia* 1984; **39**: 1168-71.
3. TAYLOR MB, GROUNDS RM, MULROONEY PD, MORGAN M. Ventilatory effects of propofol during induction of anaesthesia. Comparison with thiopentone. *Anaesthesia* 1986; **41**: 816-20.
4. PALAZZO MGA, STRUNIN L. Review article. Anaesthesia and emesis. I. Etiology. *Canadian Anaesthetists' Society Journal* 1984; **31**: 178-87.
5. BELLVILLE JW, BROSS IDJ, HOWLANDS WS. Postoperative nausea and vomiting. IV. Factors related to postoperative nausea and vomiting. *Anesthesiology* 1960; **21**: 186.
6. MADEJ TH, SIMPSON KH. Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following gynaecological surgery in day cases. *British Journal Anaesthesia* 1986; **58**: 879-83.
7. DUNDEE JW, NICHOL RM, MOORE J. Studies of drugs given before anaesthesia. III. A method for the study of their effects on postoperative vomiting and nausea. *British Journal of Anaesthesia* 1962; **34**: 527-35.
8. CLARKE RSJ. Nausea and vomiting. *British Journal of Anaesthesia* 1984; **56**: 19-27.
9. ALEXANDER GD, SKUPSKI JN, BROWN EM. The role of nitrous oxide in postoperative nausea and vomiting (Abstract). *Anesthesia and Analgesia* 1984; **63**: 177.
10. MUIR JJ, WARNER MA, OFFORD KP, BUCK CF, HARPER JV, KUNKEL SE. Role of nitrous oxide and other factors in postoperative nausea and vomiting. A randomised and blinded prospective study. *Anesthesiology* 1987; **66**: 513-18.
11. ZUURMOND WWA, VAN LEEWEN L, HELMERS JHJH. Recovery from propofol infusion as the main agent for outpatient arthroscopy. A comparison with isoflurane. *Anaesthesia* 1987; **42**: 356-9.
12. HERREGODS L, ROLLY G, VERSICHELEN L, ROSSEEL MT. Propofol combined with nitrous oxide-oxygen for induction and maintenance of anaesthesia. *Anaesthesia* 1987; **42**: 360-5.

Mood evaluation and outpatient anaesthesia

A comparison between propofol and thiopentone

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P. K. KEANE

Summary

Mood state was evaluated in 40 unpremedicated patients who underwent minor gynaecological surgery, before and up to 4 hours after, anaesthesia induced with either propofol 2.5 mg/kg or thiopentone 5 mg/kg. Assessments were made by a self-report technique, the profile of mood states method. The results indicate that mood state was less affected postoperatively in patients induced with propofol than with thiopentone. The overall impression of the investigators was that propofol patients had a definite sense of well-being after anaesthesia.

Key words

Anaesthesia; outpatient.
Anaesthetics, intravenous; propofol, thiopentone.

Outpatient anaesthesia continues to gain in popularity.¹ Propofol, when used for induction of anaesthesia, is associated with a rapid postoperative recovery and minimal postoperative sequelae.¹ The clinical impression of the investigators in the latter study was that the propofol patients had a definite sense of well-being after anaesthesia, so this study evaluated and compared mood status between propofol and thiopentone induction in patients who had outpatient minor gynaecological procedures.

Methods

Forty patients of ASA grade 1 or 2 scheduled for minor gynaecological procedures were studied with ethical committee approval and informed consent. Patients were randomly allocated to receive either thiopentone 5 mg/kg or propofol 2.5 mg/kg for induction of anaesthesia. Anaesthesia was maintained with 66% nitrous oxide in oxygen with enflurane 1-2% as required.

Mood was assessed 1 hour before operation and at 30 minutes, 1, 2 and 4 hours after operation by means of a self-report technique, the profile of mood states (POMS) method.² Recovery time from withdrawal of the anaesthetic gases to eye opening on verbal command, was noted for each patient. The postoperative data were analysed using repeated measures of analysis of covariance with the mood scores before operation as covariate.

Results

The two groups were comparable with respect to age and weight. The duration of anaesthesia was significantly shorter in the propofol group and recovery times were significantly longer after thiopentone induction (Table 1).

Table 1. Patient data, recovery times and duration of anaesthesia. Values expressed as mean (SEM).

	Propofol (n = 20)	Thiopentone (n = 20)
Age, years	44 (2.1)	44 (1.9)
Weight, kg	63 (2.1)	64 (1.5)
Duration of anaesthesia, minutes	8.4 (0.8)	11.9 (0.7)**
Recovery time, minutes	4.2 (0.3)	7.8 (0.8)***

** p < 0.01, *** p < 0.001, independent t-tests.

Significant treatment differences in mood were found for all the POMS subscales and for overall global mood disturbance (GMD) scores (Table 2). Differences in global mood disturbance scores were particularly marked at 30 minutes after operation, with a four-fold increase in GMD score in the thiopentone group compared to almost no change from baseline in the propofol patients.

These results indicate that patients who had a propofol induction were significantly less anxious, hostile, fatigued, confused, depressed and more vigorous after anaesthesia

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Table 2. Profile of mood states and global mood disturbance scores. Values expressed as mean (SEM).

		Pre-operative	0.5 hours	1 hour	2 hours	4 hours
Profile of mood states						
Anxiety	Propofol	5.9 (1.0)	2.5 (0.5)	2.5 (0.4)	1.7 (0.3)	1.1 (0.2)
	Thiopentone	3.9 (0.8)	4.4 (0.6)	2.7 (0.4)	1.7 (0.4)	1.4 (0.3)*
Hostility	Propofol	0.04 (0.1)	0.3 (0.1)	0.1 (0.1)	0.1 (0.1)	0.0
	Thiopentone	0.17 (0.1)	0.4 (0.1)	0.6 (0.2)	0.2 (0.1)	0.2 (0.1)*
Depression	Propofol	2.2 (0.7)	1.1 (0.3)	0.6 (0.2)	0.5 (0.1)	0.2 (0.1)
	Thiopentone	1.7 (0.4)	2.7 (0.5)	2.0 (0.4)	1.4 (0.3)	1.4 (0.3)***
Confusion	Propofol	2.1 (0.5)	4.1 (0.8)	2.9 (0.7)	1.2 (0.2)	0.7 (0.2)
	Thiopentone	1.8 (0.4)	6.6 (0.9)	4.3 (0.5)	2.8 (0.4)	1.8 (0.3)**
Fatigue	Propofol	1.3 (0.3)	2.3 (0.3)	1.2 (0.3)	0.4 (0.1)	0.1 (0.1)
	Thiopentone	0.9 (0.2)	4.3 (0.6)	2.7 (0.4)	1.9 (0.3)	1.4 (0.5)
Vigour	Propofol	3.6 (0.6)	1.6 (0.7)	2.3 (0.5)	4.2 (0.7)	6.8 (0.6)
	Thiopentone	4.9 (0.7)	0.4 (0.2)	1.2 (0.4)	2.1 (0.4)	3.9 (0.5)
Global mood disturbance	Propofol	8.0 (2.1)	8.6 (2.0)	4.9 (1.5)	-0.3 (1.2)	-4.6 (0.9)
	Thiopentone	3.5 (1.7)	18.2 (1.9)	11.3 (1.4)	5.7 (1.2)	2.3 (1.4)***

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, significant postoperative treatment differences, repeated measures analysis of variance with baseline values as covariate.

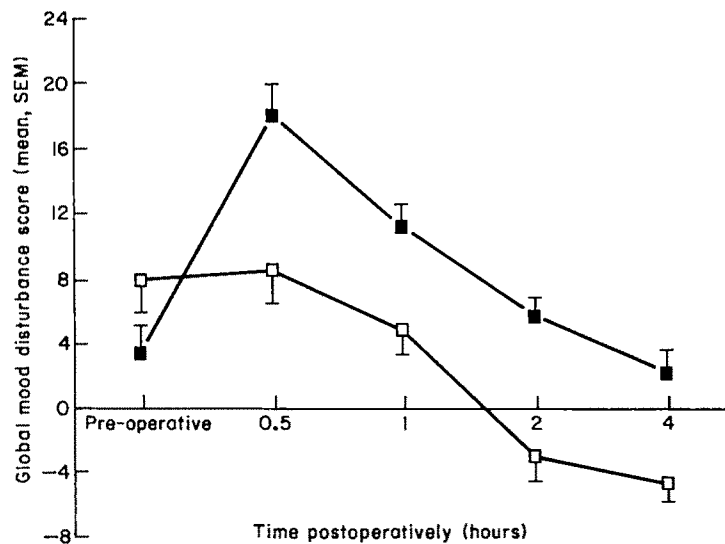


Fig. 1. Global mood disturbance scores (mean, SEM) pre-operatively and at 30 minutes, 1, 2 and 4 hours postoperatively after thiopentone and propofol induction. Postoperative treatments were significantly different at $p < 0.001$ (repeated measures analysis of variance with baseline values as covariate). ■, Thiopentone; □, propofol.

compared to patients who received a thiopentone induction.

Discussion

The effect of induction agents on postoperative psychomotor performance is well documented^{1,3} but no information is available about the effect on mood status. The results of this study indicate that postoperative mood state as measured by a well-recognised method of quantitative assessment,² is considerably less affected after a propofol induction compared to thiopentone induction. This is most probably explained by pharmacokinetic differences between the drugs, since propofol has a shorter elimination half-life,⁴ but it is possible that propofol may have a specific effect on mood centres within the central nervous system. The possibility that the shorter duration of anaesthesia in the propofol group may have influenced the mood scores postoperatively, is unlikely but cannot be excluded.

This study has demonstrated that the patients' sense of well-being is significantly better after a propofol induction for short gynaecological procedures, than after a thiopentone induction.

References

- O'TOOLE DP, MILLIGAN KR, HOWE JP, MCCOLLUM JSC, DUNDEE JW. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia. *Anaesthesia* 1986; **42**: 373-6.
- MACKAY C, COX T, BURROWS G, LAZZERINI T. An inventory for the measurement of self-reported stress and arousal. *British Journal of Social and Clinical Psychology* 1978; **17**: 283-4.
- GRANT IS, MACKENZIE N. Recovery following propofol anaesthesia—a review of three different anaesthetic techniques. *Postgraduate Medical Journal* 1985; **61**: 133-7.
- ADAMS HK, BRIGGS LP, BAHAR M, DOUGLAS EJ, DUNDEE JW. Pharmacokinetic evaluation of ICI 35 868 in man. Single induction doses with different rates of injection. *British Journal of Anaesthesia* 1983; **55**: 97-103.

Forum

Multicentre study of propofol in day case surgery

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Summary

An open multicentre study that involved 879 patients was set up after the launch of propofol to examine its use outside of the clinical trial programme and within the context of a routine clinical setting. Propofol was assessed as the main anaesthetic agent for a range of day case surgery that included gynaecological, urogenital, body surface, orthopaedic and dental procedures. For the purposes of the study, supplementary agents were restricted to fentanyl, alfentanil or nitrous oxide; no volatile anaesthetics were allowed. Induction of anaesthesia was smooth; 91.6% of patients experienced no excitatory or other adverse effect. The mean duration of anaesthesia was 12 minutes 12 seconds and the mean dosage of propofol was 10.6 mg/kg/hour. Maintenance was uneventful in the large majority of patients. Pain on injection affected approximately 25% of patients and the incidence was reduced when large veins were used for injection. Recovery was rapid with a short interval of approximately 1 minute between awakening and orientation (time to giving correct date of birth). There was a low incidence of postoperative nausea and vomiting.

Key words

Anaesthesia; outpatient.

Anaesthetics, intravenous; propofol.

There is an increasing trend towards performing short procedures on a day case basis. Patients must be ready for discharge within hours of such a procedure so a major requirement for day case surgery is rapid, complete recovery from anaesthesia.

Clinical trials have shown that recovery after anaesthesia with propofol is generally rapid and without troublesome side effects. Thus, it seemed germane to set up a post-launch study to examine its use in the routine clinical setting of day case surgery. The study assessed propofol given in intermittent bolus doses as the main anaesthetic agent for a range of elective day case procedures scheduled to last less than 30 minutes.

Methods

The study was an open multicentre trial and involved 93 anaesthetists from 87 centres. Each anaesthetist who participated was asked to recruit 10 male or female day case patients aged between 18 and 65 years and classified as ASA grade 1 or 2. All patients gave informed consent and the study protocol was approved by hospital ethical committees.

The exclusion criteria were serious impairment of respiratory, cardiovascular, hepatic, renal, haemopoietic or endocrine function; known allergy to the trial medication or previous adverse experience of general anaesthesia; pregnancy or possible pregnancy, unless this was to be terminated; and gross obesity. Patients receiving drugs which might influence the course of the anaesthetic were excluded, as were those who underwent procedures that required controlled ventilation of the lungs.

The only drugs allowed before induction of anaesthesia were atropine, fentanyl or alfentanil. Anaesthesia was induced by injection of propofol into a peripheral vein until clinical signs indicated the onset of unconsciousness. No

restriction was placed on the use of lignocaine. Anaesthesia was maintained by incremental doses of propofol as required in response to clinical signs of lightening anaesthesia. The only supplementary agents allowed were nitrous oxide, fentanyl or alfentanil; volatile anaesthetics were not permitted.

Recovery times were recorded from the administration of the last dose of propofol to when patients could open their eyes to when they could give their date of birth correctly. Any adverse effect that occurred during anaesthesia or recovery was noted. Particular attention was paid to the frequency of pain on injection and the incidence and duration of apnoea. Anaesthetists were asked to state whether any possible adverse reaction was considered to be of major clinical significance.

Results

A total of 879 patients were entered into the study 625 females (mean age 38.5 years, SD 12.8) and 254 males (mean age 43.2 years, SD 13.7). There were 19 withdrawals; in 18 cases this was due to need for volatile anaesthetics during maintenance of anaesthesia. The 860 patients who completed the study underwent a wide range of operative procedures (Table 1) and these ranged in mean duration

Table 1. Range of operative procedures and their mean durations.

Procedure	Percentage of patients	Mean (SE) duration, minutes
Body surface	9	25.1 (1.4)
Dental	1	12.6 (1.8)
Gynaecology	41	13.2 (0.2)
Orthopaedic	5	18.0 (1.6)
Urogenital	5	19.0 (0.8)
Urology	19	15.5 (0.5)
Other	20	15.9 (0.6)

Table 2. Number (%) of patients who received pre-induction drugs.

Drug	Number of patients	(%)
Atropine	31	(3.5)
Alfentanil	263	(30.6)
Fentanyl	275	(31.3)
Atropine plus fentanyl	50	(5.7)
Atropine plus alfentanil	35	(4.0)
None	220	(24.4)
Incomplete data	4	(0.5)

from 12.6–25.1 minutes. The number of patients who received pre-induction drugs is shown in Table 2.

Induction. There was a tendency for the induction dose (mg/kg) to decrease with increasing weight and an accompanying trend towards an increase in induction time (Table 3). Induction was notably smooth; 91.6% of patients experienced no excitatory or other adverse effect (Table 4). Hiccough occurred most frequently (2.4%) in the remaining patients, followed by twitching (1.4%), flushing (1.1%) and movement (1.0%). Episodes of apnoea that lasted longer than 30 seconds occurred in 19.9% of patients. There was a trend towards a higher frequency of episodes of this duration in patients who received opioids (Table 5).

Table 3. Variation in induction time and induction dose for different weight ranges.

Weight range	Number	Mean (SE) induction time, seconds	Mean (SE) induction dose, mg/kg
< 50 kg	33	45.2 (2.6)	2.4 (0.1)
	457	59.2 (1.4)	2.3 (<0.1)
70–89.9 kg	264	60.7 (1.9)	2.1 (<0.1)
> 90 kg	63	67.8 (5.4)	1.5 (0.1)

Table 4. Incidence (% of patients) of miscellaneous side effects during anaesthesia.

	Induction	Maintenance	Recovery
Bronchospasm	0.1	0.2	0.0
Confusion	NA	NA	2.2
Cough	0.8	1.7	2.0
Depression/crying	NA	NA	4.4
Elation/euphoria	NA	NA	12.2
Flush	1.1	0.8	0.3
Headache	NA	NA	3.5
Hiccough	2.4	0.7	0.0
Hypertonus	0.8	0.6	NA
Laryngospasm	0.1	0.3	0.0
Masseter spasm	0.0	0.1	0.0
Movement	1.0	0.9	NA
Nausea	NA	NA	2.3
Restlessness	NA	NA	1.5
Tremor	0.7	0.1	NA
Twitching	1.4	1.2	NA
Vomiting	NA	NA	1.5
None	91.6		75.1

NA, Not assessed.

Table 6. Number (%) of patients who experienced pain on injection.

Site of injection	Number (%) of painful injections
Antecubital fossa	
With lignocaine 6	0(0.0)
Without lignocaine 122	6(4.2)
Forearm	
With lignocaine 18	4(22.2)
Without lignocaine 43	5(11.6)
Hand	
With lignocaine 205	54(26.3)
Without lignocaine 457	152(33.2)
Total	
With lignocaine 229	58(25.3)
Without lignocaine 622	163(26.2)

* In 28 cases either the injection site or the use of lignocaine was unspecified.

Table 6 shows the sites used for injection of propofol. Pain on injection into a vein in the dorsum of the hand occurred in 31% of patients (206/662), while the incidence for injection into a vein in the forearm or antecubital fossa was 7.9% (15/189). There was no apparent trend in the occurrence of pain associated with the use of lignocaine in 229 patients. Quality of induction was assessed as good in 80.3% of patients, adequate in 17.5% and poor in 1.7% (it was not specified in 0.5% of patients).

Maintenance. A single dose of propofol was sufficient for completion of the surgical procedure in 118 patients. The mean duration of the procedure in this group was 6.2 minutes. The remaining patients required additional doses of propofol and there was a wide variation in the size of the incremental dose (Fig. 1). The number of increments and the total dose showed a direct relationship to the duration of anaesthesia (Fig. 2). The mean duration of the procedure was 12 minutes 12 seconds for these patients and the mean rate of utilisation of propofol was 10.6 mg/kg/hour. Nitrous oxide was used in 87% of patients and 24.2% received opioids during maintenance.

Maintenance was generally uneventful and there were no excitatory or other adverse effects in 93.5% of patients. The most common effects were cough (1.7%) and twitching (1.2%) (Table 4). Only one possible adverse reaction was identified by the anaesthetists to be of major clinical significance. This was a case of hyperventilation. Anaesthetists graded the quality of maintenance as good or adequate in 91.7%, and poor or inadequate in 7.4%.

Recovery. Times until patients awakened and could give their correct date of birth are presented in Table 7. More than 50% of patients were able to give correct date of birth within 8 minutes of the final dose of propofol. Particularly noteworthy is the observation that there was a short interval between the two indices of recovery, of approximately one minute. The overall incidence of unpleasant or troublesome effects during recovery was low: only 1.5% of patients vomited postoperatively and a further 2.3% suffered from nausea. Most frequently reported during recovery was a feeling of elation/euphoria (Table 4).

Table 5. Number (%) of patients who experienced apnoea on induction.*

Regimen for induction	Apnoea > 30 seconds	Apnoea < 30 seconds	No apnoea	Total
Propofol and alfentanil	74(24.8%)	61(20.5%)	163(54.7%)	298
Propofol and fentanyl	77(23.7%)	57(17.5%)	191(58.8%)	325
Propofol alone	24 (9.5%)	53(21.0%)	175(69.4%)	252
Total	175(19.9%)	171(19.4%)	529(60.4%)	875

* Four patients are excluded because of incomplete data.

Table 7. Recovery times from last dose of propofol.

	To open eyes on command		To give correct date of birth	
	Median	90% Range	Median	90% Range
Propofol alone (<i>n</i> = 79)	6'31"	3'0"-12'00"	7'38"	3'27"-15'20"
Propofol and nitrous oxide (<i>n</i> = 550)	6'30"	3'13"-14'10"	7'15"	3'34"-15'33"
Propofol and alfentanil (<i>n</i> = 146)	6'44"	2'52"-15'03"	7'27"	3'32"-16'27"
Propofol and fentanyl (<i>n</i> = 57)	8'05"	2'42"-21'36"	8'57"	2'53"-22'57"

Times given as minutes (') and seconds(").

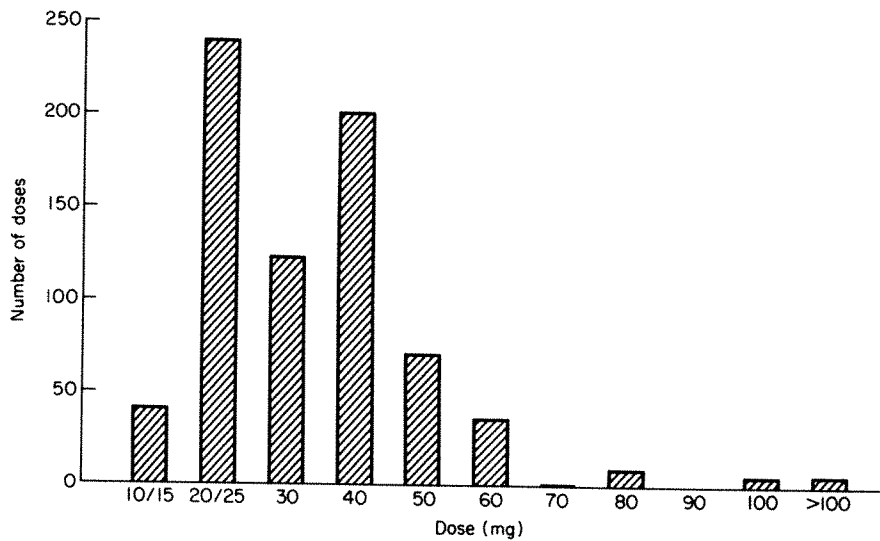


Fig. 1. Variation in incremental doses of propofol.

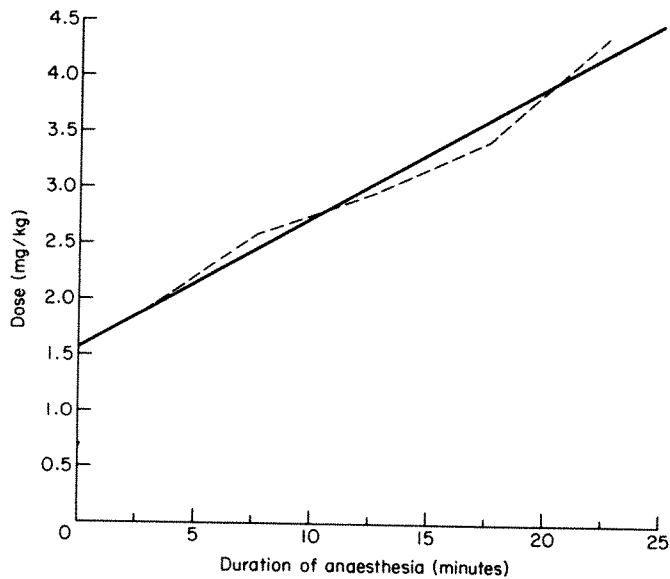


Fig. 2. Variation in maintenance doses of propofol. ---, Maintenance dose; —, regression line.

Discussion

This post-launch study conducted in 879 patients enabled anaesthetists unfamiliar with propofol to employ it as the main anaesthetic agent in a routine clinical setting. Propofol provided a high quality of induction and maintenance under these conditions, comparable to that reported in controlled clinical trials. The data also confirm that the

drug can be used satisfactorily in standard techniques with nitrous oxide, fentanyl and alfentanil. The results of this study are consistent with previous reports that the incidence of pain on injection can be minimised by the choice of large veins for injection of propofol. The frequent use of veins in the hand as the injection site for anaesthetic agents is partly related to the

known risks of inadvertent intra-arterial injection of thiopentone.¹ No tissue damage was reported after accidental intra-arterial injection of propofol.² Lignocaine was used by some investigators to avoid pain on injection. The study itself was not designed to assess the efficacy of lignocaine, no specific guidance on its use was given and no trend emerges from retrospective analysis of the data. There are, however, reports in the literature^{3,4} that lignocaine can minimise the incidence of pain on injection of propofol into small veins.

The present data confirm the results of previously published trials that recovery after anaesthesia with propofol is rapid and patients are clear-headed; these are important features for day case anaesthesia. An interesting observation that requires further study was the number of patients described as elated/euphoric during recovery. It may be questioned whether anaesthetists are so used to patients feeling hungover after anaesthesia that a feeling of well-being is described as elation.

Conclusions

The results of this large multicentre study confirm that propofol is highly suitable for use as the main anaesthetic agent in day case surgery. It provides a good quality of anaesthesia with rapid recovery and patients are clear-headed and generally untroubled by unpleasant side effects.

References

1. KAY B. Propofol in anaesthesia. *Lancet* 1987; **2**: 334.
2. CHONG M, DAVIS TP. Accidental intra-arterial injection of propofol. *Anaesthesia* 1987; **42**: 781.
3. BROOKER J, HULL CJ, STAFFORD M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40**: 91-2.
4. STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 152-6.

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The effect of fentanyl on propofol requirements for day case anaesthesia

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Summary

Fifty women of ASA grade 1 or 2 scheduled to undergo minor gynaecological procedures were allocated randomly to two groups. Group A received fentanyl 100 µg intravenously before induction; group B received no sedative or analgesic drugs. Anaesthesia was induced with propofol intravenously and maintained using 67% nitrous oxide in oxygen with incremental doses of propofol. Induction time and dose were significantly less and mean arterial pressure decreased significantly lower in Group A. These differences were, however, small and the ranges of values were large. The incidence of side effects and subjective assessment of quality of anaesthesia were similar in both groups. Fentanyl did not confer any practical advantage when used with propofol in the techniques described above.

Key words

Anaesthesia; outpatient.
Anaesthetics, intravenous; propofol.
Analgesics, narcotic; fentanyl.

Propofol, since its release for general use in 1986, has become a popular drug for induction of anaesthesia for short procedures, particularly in day patients where its short duration of action is especially advantageous.¹ Induction may be followed by maintenance using propofol by infusion^{2,3} or incrementally; alternatively, a volatile agent may be used.

Short-acting opioids are often used for day patient anaesthesia as part of a balanced technique but there is no published work on the effect of opioids on the dose required or on the quality of anaesthesia with propofol. This study set out to examine the effects of fentanyl in such a situation.

Patients and methods

Fifty women aged 18-65 years of ASA grade 1 or 2 who were to have minor gynaecological procedures as day patients were eligible for inclusion in the study, which was approved by the District Ethical Committee. No premedication was given and patients were allocated randomly to one of two groups: group A received fentanyl 100 µg intravenously 1-5 minutes before induction of anaesthesia, while

group B received no fentanyl. Anaesthesia was induced with propofol 1.5 mg/kg intravenously over 20 seconds and then a further dose titrated slowly until loss of consciousness. Maintenance was with 67% nitrous oxide in oxygen with increments of propofol 20-50 mg as needed.

Blood pressure was recorded before induction, 2 minutes after induction and at intervals thereafter using a non-invasive oscillometric device (Critikon Dinamap 845). Heart rate was recorded from an ECG (lead CM5). The induction dose and time taken, untoward events and a subjective assessment of quality of induction were recorded, as were the presence and duration of apnoea.

Maintenance doses and timing, untoward events such as movement, and a subjective assessment of control of depth of anaesthesia were noted by the anaesthetist. The duration of surgery was recorded together with the time from start of induction to the end of surgery (the anaesthetic time). Recovery time was measured from the last dose of propofol to ability to open eyes in response to command. Ability to give date of birth accurately was taken to be an indication of orientation. Untoward events during recovery were also noted and, before discharge, patients were interviewed to

ascertain whether they had been aware during the procedure and asked whether they would choose to receive the same anaesthetic again.

Results

The characteristics of the two groups are shown in Table 1. There were no significant differences in age, weight or duration of anaesthesia.

Table 2 compares induction times, doses for induction and maintenance and recovery times. Induction time and dose were significantly less in group A but differences between maintenance doses and recovery times were not significant. Table 3 shows cardiovascular changes during induction; mean arterial pressure decreased significantly more in Group A but heart rate was not significantly different. The ranges of blood pressure and heart rate were wide. The subjective assessments of quality of induction and movement are given in Table 4. Differences were not significant.

The incidence of side effects during induction, notably pain on injection, was low in both groups and differences were not significant. The incidence and duration of apnoea after induction were not significantly different between groups. Four patients were apnoeic for more than 60 seconds; all had received fentanyl. Postoperative side effects were uncommon, with no significant differences between groups; two patients in group B were nauseated and one patient in group A vomited.

Table 1. Details of patients.

	Group A (fentanyl) (n = 25)	Group B (no fentanyl) (n = 25)
Mean (SD) age, years	36.3 (11.5)	36.6 (11.2)
Mean (SD) weight, kg	68.6 (12.7)	64.5 (11.0)
Mean (SD) duration of anaesthesia, minutes	8.2 (2.6)	9.2 (4.3)

No significant differences between groups (Student's *t*-test).

No patient was aware during the procedure and one in each group said they would not choose a similar anaesthetic again. All patients went home on the same day as the procedure.

Discussion

Premedication with fentanyl 100 µg did not have a useful effect on the quality of the anaesthetic induction with propofol. The quality of induction was good in most cases (80%), despite a significant decrease in induction time and propofol dose with the use of fentanyl. The incidence of side effects was low; 8% of patients experienced discomfort on injection, compared to about 30% in some other studies.⁴ The greater decrease in mean blood pressure after induction in the fentanyl group did not pose a clinical problem although it was statistically significant, and no patient required any treatment.

Fentanyl had no useful effect on the maintenance of anaesthesia with intermittent propofol; it neither improved control of depth of anaesthesia nor significantly reduced the dose of propofol. The majority of patients moved during the surgical procedure and the control of anaesthetic depth was generally considered to be adequate rather than

Table 4. Subjective assessments in the two groups.

	Group A (fentanyl) (n = 25)	Group B (no fentanyl) (n = 25)
<i>Quality of induction</i>		
Good	22	20
Adequate	2	3
Poor	1	2
<i>Movement during procedure</i>		
None	10	8
Slight	6	9
Moderate	9	8

No significant difference between groups (Mann-Whitney *U*-test).

Table 2. Induction times and doses, maintenance rates and recovery times in the two groups.

	Group A (fentanyl) (n = 25)	Group B (no fentanyl) (n = 25)	95% confidence interval of difference between means
Mean (SD) induction time, minutes	50.1 (14.1)	61.7 (17.7)*	2.6-20.6
Mean (SD) induction dose, mg/kg	1.98 (0.43)	2.26 (0.38)†	0.05-0.51
Mean (SD) maintenance rate, µg/kg/minute	0.153 (0.068)	0.188 (0.068)	—
Mean (SD) recovery time, minutes	6.0 (2.0)	6.1 (1.7)	—

* *p* < 0.02, † *p* < 0.05, significant differences between groups. (Student's *t*-test)

Table 3. Cardiovascular changes in the two groups, from before induction to 2 minutes after.

	Group A (fentanyl) (n = 25)	Group B (no fentanyl) (n = 25)	95% confidence interval of difference between means
<i>Blood pressure change, mmHg</i>			
Mean (SD)	-9.6 (12.3)	-2.2 (12.6)*	0.03-14.5
Range	+15 to -30	+23 to -42	
<i>Heart rate change, beats/minute</i>			
Mean (SD)	-7.7 (11.5)	-2.5 (15.2)	—
Range	+11 to -25	+22 to -20	

* *p* < 0.05, significant difference between groups (Student's *t*-test).

good; the surgical procedures were not affected adversely. The procedures were of short duration so only small doses of propofol were required to maintain anaesthesia.

The recovery times were brief (the majority were about 5 minutes) with almost immediate return to orientation and this was not affected adversely by the use of fentanyl. The rapid recovery together with the low incidence of side effects during recovery in both groups, does not prejudice the use of fentanyl with propofol as a day case technique.

In conclusion, fentanyl was not found to confer any clinical advantages on the use of intermittent propofol as an anaesthetic technique in short, relatively painless, gynaecological day case procedures.

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Use of propofol for sedation during gastrointestinal endoscopies

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Summary

This study investigated the suitability of propofol as a sole agent for continuous sedation in 100 unpremedicated patients during gastrointestinal endoscopy. The propofol was given very slowly (average 62.7 seconds) in order to prevent apnoea during induction, and the dose adjusted according to age (68% of patients were older than 50 years) and ASA grade (32% were ASA grade 3 or 4). There was no correlation under these circumstances between the observed haemodynamic variations and the age or ASA grade of the patients. The infusion rate during maintenance was also adjusted for age, and for the type of endoscopy. The mean rate was 4.3 mg/kg/hour. Recovery was rapid and of excellent quality; 77 patients were awake within 10 minutes and 99 reported total amnesia.

Key words

*Anaesthetics, intravenous; propofol.
Surgery; endoscopy.*

The aim of this study was to determine the dose of propofol required to induce and maintain adequate sedation to permit any type of examination of the digestive tract. Propofol was the sole sedative agent.

Methods

One hundred patients (47 male), of whom 40 were day cases, were scheduled in this open study to undergo endoscopy of the digestive tract. Their mean age was 58.7 years (range 20–93). All gave informed oral consent. Only children and pregnant women were not studied and therefore there was a relatively high number of patients of ASA grade 3 (ASA grade 1, 33; grade 2, 35; grade 3, 30; grade 4, 2). The types of examination are shown in Table 1.

The gastroenterologists who perform the endoscopies in this unit prefer their patients to be able to respond to pain. Therefore the desired level of sedation was to maintain the patient unconscious but able to respond to painful stimuli and yet to have no memory of the event.

A cannula was inserted into a vein in the dorsum of the hand or forearm. Arterial blood pressure was measured indirectly before and 2 minutes after the injection of propofol and every 2 minutes thereafter during maintenance. Heart rate was recorded at the same times. The throat of the patients was sprayed with 5% lignocaine, depending on the type of endoscopic examination.

References

1. HENRIKSSON B-Å, HALLÉN B, HÄGERDAL M, KARLSSON P, LUNDBERG D, PONTÉN J. Propofol vs thiopentone as anaesthetic agents for short operative procedures. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 63–6.
2. SPELINA KR, COATES DP, MONK CR, PRYS-ROBERTS C, NORLEY I, TURTLE MJ. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1986; **58**: 1080–4.
3. DOZE VA, WESTPHAL LM, WHITE PF. Comparison of propofol with methohexital for outpatient anaesthesia. *Anesthesia and Analgesia* 1986; **65**: 1189–95.
4. MCCOLLUM JSC, DUNDEE JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41**: 995–1000.

Table 1. Types of gastrointestinal examination and distribution of patients.

Type of examination	Number of patients
Gastroscopy	60
Gastroscopy with sclerosis of oesophageal varices	10
Gastroscopy with oesophageal dilatation*	8
Total colonoscopy	8
Cholangiopancreatography	
Without sphincterotomy†	10
With sphincterotomy*	3
Transcutaneous liver biopsy	1
Total	100

* Examination considered to be particularly painful.

† Examination considered to be painful.

The induction dose was titrated to the desired level according to age and ASA grade, and was given slowly. Three arbitrarily chosen age groups were considered: ≤ 50 years, 51–74 years and ≥ 75 years. Maintenance of sedation was started immediately after induction by a continuous infusion of propofol given by syringe pump. The infusion rate was chosen according to age and to the type of examination and was adjusted and/or supplementary bolus doses of propofol given in cases of inadequate sedation.

The patients breathed air throughout the procedure. The

propofol infusion was stopped at the end of the examination and all except the patient who had a liver biopsy were placed in the left lateral decubitus position. The times from the end of the infusion until the patients were able to open their eyes and until they were orientated in time and space, were noted. The Steward score¹ was used to assess the quality of recovery. All the patients were supervised for at least one hour in the recovery room. Side effects that occurred during induction, maintenance and recovery were noted.

Statistical analysis of the haemodynamic variations was done using two-tailed paired Student's *t*-tests; *p* values <0.05 were regarded as significant. Subroutines of the

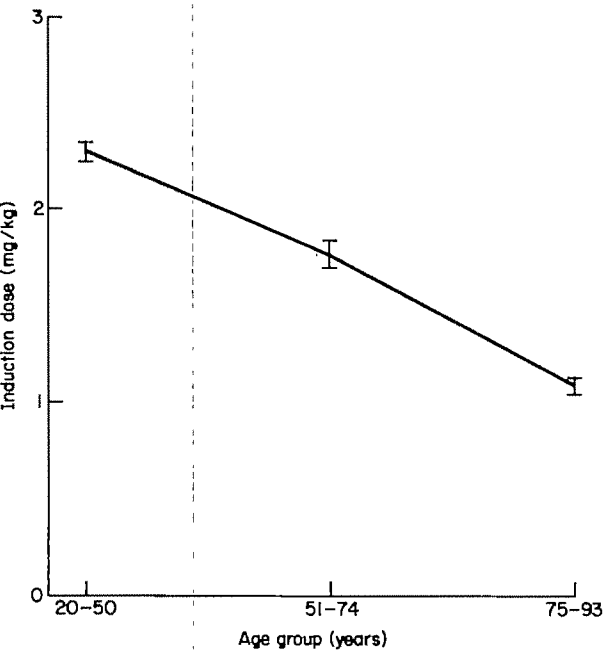


Fig. 1. Mean (SEM) induction doses of propofol in the three age groups 20-50 years (*n* = 32), 51-74 years (*n* = 43) and 75-93 years (*n* = 25).

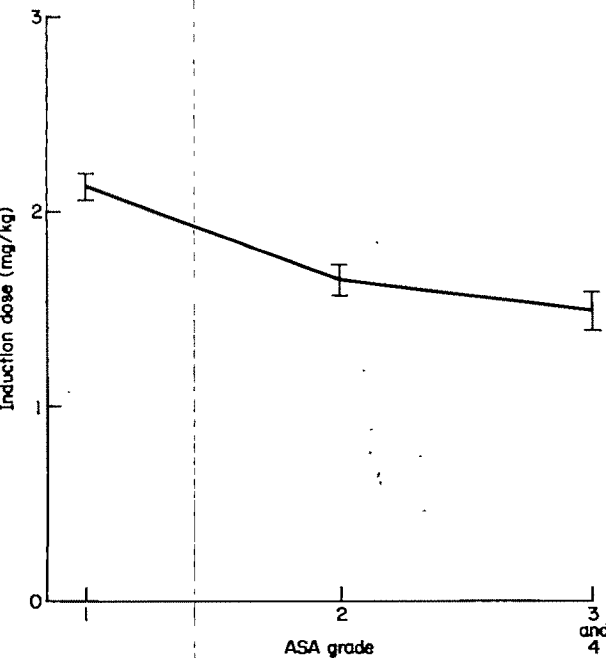


Fig. 2. Mean (SEM) induction doses of propofol for patients of ASA grades 1 (*n* = 32), 2 (*n* = 35) and 3 and 4 (*n* = 32).

Table 2. Variations at induction of systolic, diastolic and mean arterial pressure and heart rate.

	Baseline measurements	2 minutes after propofol
Arterial pressure (mmHg)		
Systolic	141.29	111.19* (-20.19%)
Diastolic	86.16	70.90* (-16.21%)
Mean	104.06	84.14* (-17.90%)
Heart rate, beats/minute	87.65	87.28

* Significantly different from measurement before induction (*p* < 0.001).

Table 3. Side effects at induction related to duration of injection and to dose.

Side effect	Duration of injection < 30 seconds	Induction dose > 2.5 mg/kg
Muscular hypertonus (<i>n</i> = 1)	1	0
Movement (<i>n</i> = 1)	1	1
Muscular fasciculation (<i>n</i> = 2)	0	1
Masseter spasm (<i>n</i> = 2)	0	2

Table 4. Maintenance dose of propofol related to type of endoscopic examination.

Type of examination	Mean infusion rate (mg/kg/hour)	Mean duration of sedation (minutes)
Transcutaneous liver biopsy (<i>n</i> = 1)	3	7
Gastroscopy (<i>n</i> = 60)	3.9	8.4
Cholangiopancreatography (<i>n</i> = 13)	3.8	23.4
Gastroscopy with sclerosis of oesophageal varices (<i>n</i> = 10)	4.75	14.8
Total colonoscopy (<i>n</i> = 8)	4.75	19.3
Gastroscopy with oesophageal dilatation (<i>n</i> = 8)	6.5	21.4

multifunction statistics software package STATPAK were applied where appropriate to determine correlation and least-squares coefficients of a single variable regression.

Results

Induction. The mean duration of propofol injection was 62.7 seconds (range 30-120, SD 22) and the mean dose, 1.76 mg/kg (0.8-2.9, SD 0.58). The results of titration of the induction dose according to the three age groups and ASA grade are shown in Figs 1 and 2, respectively. An exponential correlation was found between the induction dose and the age of the patients (Fig. 3). The quality of induction was assessed as good in 97 patients and adequate in three. No apnoea was observed in any patient. The variations in blood pressure 2 minutes after the injection of propofol (Table 2) were significant and corroborate the findings of other authors.

Twenty-six patients reported pain on injection; in 16 of these, propofol was injected into a vein on the dorsum of the hand and the injection was performed in less than 75 seconds. Other side effects during induction occurred when the injection was too fast (two cases out of six) and/or when the dose administered was higher than 2.5 mg/kg (four cases out of six) (Table 3).

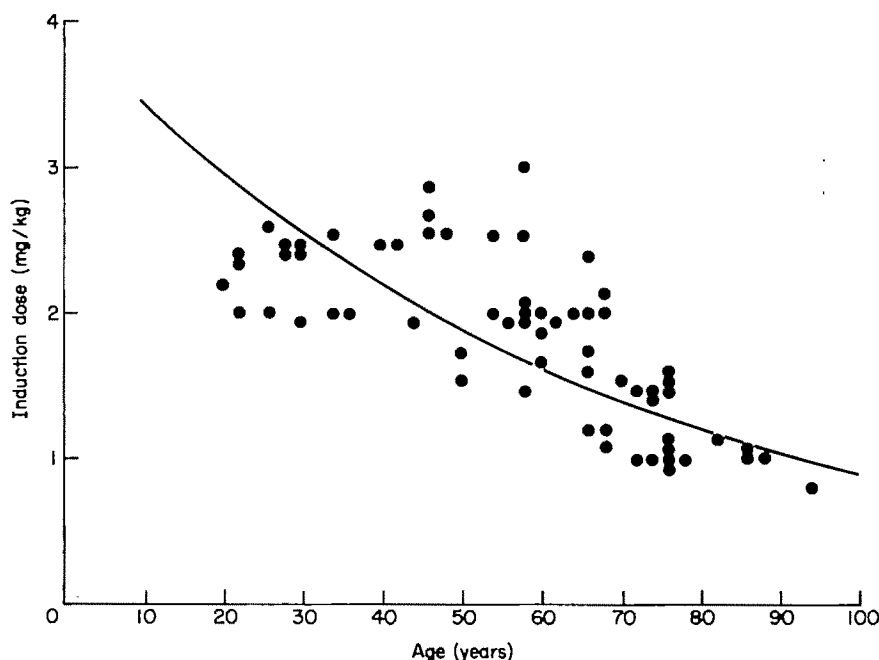


Fig. 3. Induction dose related to age of patients, showing exponential correlation.

Table 5. Quality of maintenance related to type of endoscopic examination.

Type of examination	Quality of maintenance		
	Good	Adequate	Insufficient
Gastroscopy (n = 60)	54	6	0
Gastroscopy with sclerosis of oesophageal varices (n = 10)	8	2	0
Gastroscopy with oesophageal dilatation (n = 8)	5	3	0
Total colonoscopy (n = 8)	7	0	1
Cholangiopancreatography without sphincterotomy (n = 10)	8	2	0
Cholangiopancreatography with sphincterotomy (n = 3)	1	2	0
Transcutaneous liver biopsy (n = 1)	1	0	0
Total (n = 100)	84	15	1

Maintenance. The mean rate of infusion of propofol was 4.3 mg/kg/hour (range 2–9, SD 1.4). The mean duration of sedation was 12.9 minutes (range 3.8–49.0, SD 8.57). As for the induction dose, there was an exponential correlation between infusion rate and the age of the patients (Fig. 4). The infusion rate also varied according to the type of examination, regardless of its duration (Table 4).

The quality of maintenance was judged to be good in 84 patients, adequate in 15 and inadequate in only one (Table 5). It was necessary to adjust the infusion rate and/or to administer supplementary bolus doses of propofol in 13 of the latter 16 patients. Endoscopy was painful in nine of these 13 patients and seven of them had a high alcohol intake. The infusion rate was not increased in three of the 16 patients, because of their poor general condition.

Exaggerated peristalsis was observed in 11 patients and nine of these were given 20–40 mg N-butyhyoscine. Side effects (Table 6) were few and did not interfere with the performance of endoscopy.

Recovery. The mean time between the end of the propofol infusion and opening eyes was 4.78 minutes (SD 5.92). Table 7 shows in detail the times of opening eyes related to

Table 6. Side effects during maintenance.

Side effect	Cause			Favoured by existing pathology
	Propofol	Examination	Dorsal decubitus position	
Cough (n = 24)	0	24	0	14
Hiccough (n = 7)	0	7	0	4
Upper respiratory obstruction (n = 2)	0	0	2	0
Movement (n = 1)	1	0	0	0
Redness of the vein (n = 1)	1	0	0	0
Hypersalivation (n = 11)	0	11	0	0

Table 7. Number of patients with eyes open at various times after the end of infusion, related to mean age and ASA grade.*

Time (minutes)	Number of patients	Mean age (years)	ASA grade	
			1 or 2	3 or 4
0–4	53	54.71	77.3%	22.7%
5–10	38	72.36	52.6%	47.4%
11–36	5	72.2	40.0%	60.0%

* Data for four patients who opened their eyes during examination, are excluded.

age and ASA grade. Four patients whose eyes opened during the examination are excluded, although this did not cause any problem during the normal course of the procedure.

On average patients were orientated 6.1 minutes (SD 5.73) after the end of the propofol infusion (Table 8). One patient, who was in poor general health, woke up shortly after induction and remembered the whole examination but did not regard this as a particularly unpleasant experience. This patient had undergone a laryngectomy previously, was receiving chemotherapy, had severe respiratory insufficiency and required regular oesophageal dilatation. The initial dose of propofol was clearly insufficient and was increased during subsequent treatments.

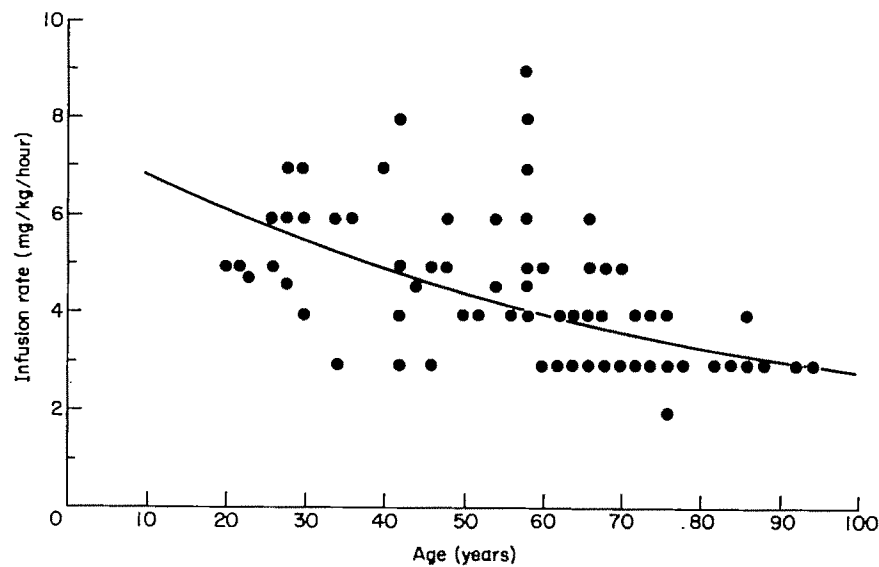


Fig. 4. Infusion rate during maintenance related to age of patients, showing exponential correlation.

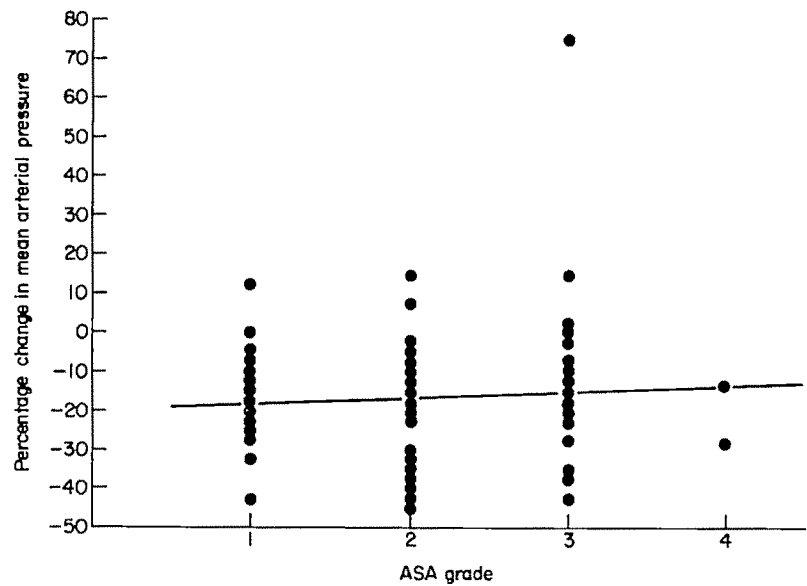


Fig. 5. Variation of mean arterial pressure 2 minutes after induction, related to ASA grade. The variations are statistically significant but do not correlate with ASA grade.

Of the patients who were orientated within the first 6 minutes, 71.6% belonged to ASA grade 1 or 2; of those who were orientated after 6 minutes, 70% were of ASA grade 3 or 4.

The maximum Steward score of 6 was reached after a mean duration of 7.9 minutes (range 1–36, SD 6.4). This was an average of 3.48 minutes after opening their eyes. Table 9 shows how the quality of recovery was related to age. Three elderly patients (mean age 78 years) woke up after a long delay (25 minutes). Ninety-nine patients reported total amnesia for the whole period of examination. The side effects observed during recovery were minimal and always of short duration. Headache, nausea, agitation and logorrhea occurred in one patient each, confusion/excitation in two and euphoria in four. The latter patients were young and the procedures short (mean duration 6.4 minutes).

Discussion

The quality of induction was assessed as good in 97 patients; the dose used was smaller than those reported in the litera-

Table 8. Number of patients orientated at various times after the end of infusion, related to mean age.

Time (minutes)	Number of patients	Mean age (years)
0–6	68	55.4
7–10	21	64.8
11–36	10	71.6

Table 9. Number of patients with Steward score of 6 at various times after the end of infusion, related to mean age.

Time (minutes)	Number of patients	Mean age (years)
1–3	23	
4–5	33	54.8
6–10	21	
11–15	20	65
25–36	3	78

ture.^{2–5} Nevertheless, a small degree of respiratory depression was observed although no apnoea was noted (defined as a respiratory arrest of 30 seconds or more). Several pre-

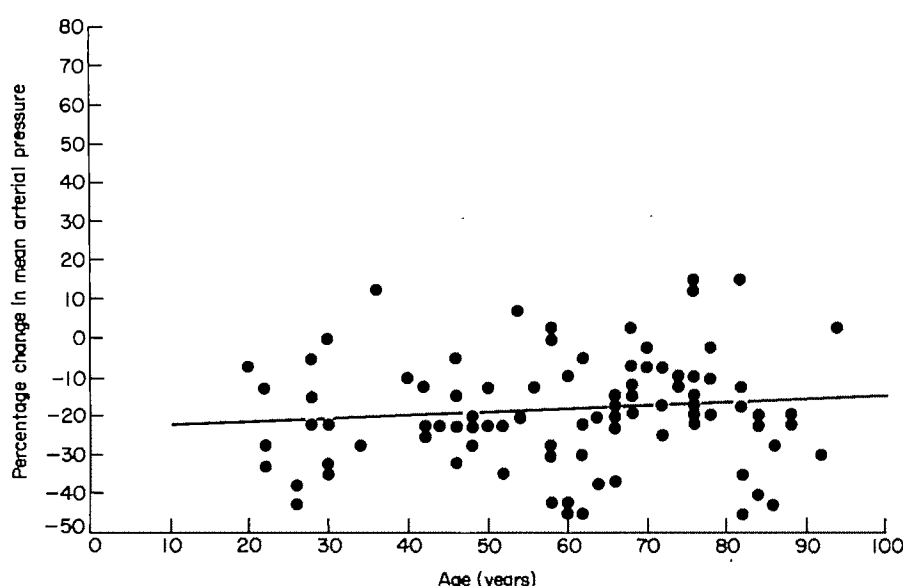


Fig. 6. Variation of mean arterial pressure 2 minutes after induction, related to age of patients. The variations are statistically significant but do not correlate with age.

cautions were taken to prevent apnoea. No premedication was used, which can influence the occurrence of apnoea.^{5,6} The incidence and duration of apnoea are minimised by slow injection of propofol.^{7,8} We also adjusted the dose according to age and ASA grade.⁷⁻⁹ A fixed induction dose that depends only on the weight of the patient, may provoke a higher incidence of apnoea.^{6,9} Elderly patients are known to be more sensitive to intravenous anaesthesia.⁹

The haemodynamic variations observed at induction corroborate those found in other studies^{10,11} and are dose dependent.¹² No correlation was found between the haemodynamic variations at induction and age or ASA grade (Figs 5 and 6). The incidence of hypotension was not higher in elderly patients or in those of ASA grade 3-4, which can be attributed to the lower dose given to these patients and to the slow speed of injection.

The mean infusion rate of propofol during maintenance was less than those reported previously.^{2,6,13} This is a reflection of the age of the patients (68% older than 50 years) and the level of sedation appropriate for the types of examinations (60 were gastroscopies which required an infusion rate of 3 mg/kg/hour compared with 6-9 mg/kg/hour for more painful endoscopies).

Servin *et al.*¹⁴ suggested an increase in the extrahepatic metabolism of propofol in patients with cirrhosis. It was noted during this study that patients with a high alcohol intake required a higher dose of propofol. The side effects observed during maintenance, such as cough and hiccough, were attributed to the procedure itself, such as the backward and forward motion of the gastroscope. The incidence was higher in those with chronic bronchitis and pyloric stenosis.

The observed mean recovery times correspond to those reported in unpremedicated patients who received propofol only.^{15,16} Duration of recovery increased slightly with increasing age and ASA grade. No correlation was observed between the total consumption of propofol and the delay in emergence^{6,10} in these endoscopies of limited duration, contrary to the findings of Redfern *et al.*¹² and probably because of variation in individual sensitivity to the drug.⁷ Three elderly patients (78, 82 and 88 years) who suffered from advanced cerebral arteriosclerosis, woke up long after the propofol infusion was stopped. Neither induction dose

(0.93-1.07 mg/kg) nor the infusion rate during maintenance can explain this delayed recovery.

It is concluded that an infusion of propofol in the manner described is a satisfactory method of sedation for patients who undergo gastrointestinal endoscopy, and is preferred to light premedication by patients who have experienced both methods.

Acknowledgments

We thank the nursing staff of the Department of Gastroenterology for their help in performing this study. We also thank ICI-Pharma (Belgium) and, in particular, Mr G. Byttebier for assistance in the statistical analysis of the results.

References

1. STEWARD DJ. A simplified scoring system for the post-operative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-3.
2. GEPTS E, VAN DE VELDE A, DEVIS G, SMEKENS L. Technique de sédation par perfusion continue de Diprivan en endoscopie digestive. *Acta Endoscopica* 1983; **13**: 93-7.
3. LOGAN MR, DUGGAN JE, LEVACK ID, SPENCE AA. Single-shot i.v. anaesthesia for outpatient dental surgery. *British Journal of Anaesthesia* 1987; **59**: 179-83.
4. MCCOLLUM JSC, DUNDEE JW. Comparison of induction characteristics of four intravenous anaesthetic agents. *Anaesthesia* 1986; **41**: 995-1000.
5. TAYLOR MB, GROUNDS RM, MULROONEY PD, MORGAN M. Ventilatory effects of propofol during induction of anaesthesia. *Anaesthesia* 1986; **41**: 816-20.
6. TURTLE MJ, CULLEN P, PRYS-ROBERTS C, COATES D, MONK CR, FAROQUI MM. Dose requirement of propofol by infusion during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1987; **59**: 283-7.
7. DUNDEE JW, ROBINSON FP, MCCOLLUM JSC, PATTERSON CC. Sensitivity to propofol in the elderly. *Anaesthesia* 1986; **41**: 482-5.
8. ROBINSON FP, DUNDEE JW, HALLIDAY NJ. Age affects the induction dose of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 157-9.
9. SEAR JW. Toxicity of i.v. anaesthetics. *British Journal of Anaesthesia* 1987; **59**: 25-45.

10. GEPTS E, CLAEYS MA, CAMU F, SMEKENS L. Infusion of propofol ('Diprivan') as sedative technique for colonoscopy. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 120-6.
11. GROUNDS RM, MORGAN M, LUMLEY J. Some studies on the properties of the intravenous anaesthetic, propofol ('Diprivan')—review. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 90-5.
12. REDFERN N, STAFFORD MA, BROOKER J, HULL J. Incremental propofol for short procedures. *British Journal of Anaesthesia* 1985; **57**: 349-50P.
13. SPELINA KR, COATES DP, MONK CR, PRYS-ROBERTS C, NORLEY I, TURTLE MJ. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. *British Journal of Anaesthesia* 1986; **58**: 1080-4.
14. SERVIN F, HABERER JP, COCKSHOTT ID, FARINOTTI R, DESMONDTS JM. Propofol pharmacokinetics in patients with cirrhosis. *Anesthesiology* 1986; **65**: 554A.
15. MACKENZIE N, GRANT IS. Propofol for intravenous sedation. *Anaesthesia* 1987; **42**: 3-6.
16. MILLIGAN KR, O'TOOLE DP, HOWE JP, CLARKE RSJ. Recovery from outpatient anaesthesia: comparison of propofol and isoflurane maintenance. *British Journal of Anaesthesia* 1987; **59**: 134P.

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Intubation under induction doses of propofol

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Summary

Twenty patients, ASA grades 1 and 2, aged 18-65 years were admitted to an open study to investigate the ease of tracheal intubation after induction of anaesthesia with propofol without the use of muscle relaxants after the chance observation that propofol 2.5 mg/kg allowed easy laryngoscopy and tracheal intubation. Satisfactory intubation conditions were achieved in 19 patients.

Key words

Anaesthetics, intravenous; propofol.
Intubation, tracheal.

Tracheal intubation is usually carried out under a combination of general anaesthesia and muscle relaxation; the latter is provided by either depolarising or non-depolarising agents. Suxamethonium is currently the only widely used depolarising agent and is the agent of choice for rapid sequence intubation, due both to its speed of onset of action and its excellent muscular relaxation. It does, however, have many undesirable side effects. The newer non-depolarising agents, atracurium and vecuronium have not, unfortunately, fulfilled the search for a rapid onset non-depolarising agent. The chance observation that laryngoscopy might easily be performed using propofol 2.5 mg/kg was thought worthy of investigation for these reasons.

Methods

Twenty adult patients, male and female, who required tracheal intubation for surgery were studied. All patients were of ASA grade 1 or 2 and aged 18-65 years. There were no contraindications to propofol and no obvious anatomical abnormalities which suggested difficult tracheal intubation. The study was approved by the hospital ethical committee and verbal consent was obtained from all patients.

Patients were premedicated with diazepam 10 mg and droperidol 5 mg one and a half hours before anaesthesia. Induction of anaesthesia was with intravenous propofol 2.5 mg/kg injected into a large vein on the forearm or dorsum of the hand, over 20 seconds. Laryngoscopy was attempted as soon as possible after loss of consciousness as assessed by loss of eyelash reflex and change in respiratory pattern. Arterial blood pressure was measured before induction of anaesthesia and 2 minutes after intubation. Anaesthesia

was maintained with oxygen, nitrous oxide and either halothane or enflurane.

Ease of intubation was graded on a three-point scale: 1, smooth and easy intubation; 2, mild coughing or bucking on intubation; 3, intubation impossible.

Results

Grade 1 intubation was achieved in 12 patients, grade 2 in seven and grade 3 in one patient who had a previously undiagnosed palatoglossal abnormality and in whom intubation proved extremely difficult even after full doses of muscle relaxants. Mean time to unconsciousness in the remaining 19 patients was 30.2 seconds (SEM 2.65) and the mean time from unconsciousness to intubation, 35.2 seconds (SEM 6.55) (Figs 1 and 2). Mean arterial blood

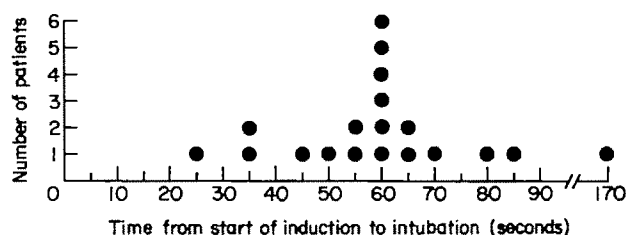


Fig. 1. Times from start of induction to intubation. For clarity, values have been rounded to the nearest 5 seconds.

pressure decreased from 93 mmHg (SEM 3.0) before induction to 88 mmHg (SEM 4.4) at 2 minutes after intubation. These changes were not significant. Two patients had sore throats at 24 hours.

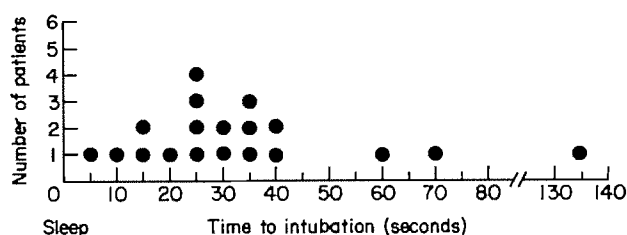


Fig. 2. Times from loss of consciousness to intubation. For clarity, values have been rounded to the nearest 5 seconds.

Discussion

Intubation may often be attempted before muscle relaxants have had sufficient time to reach maximum effect. Thiopentone alone, was shown to provide adequate conditions for intubation as long ago as 1948.¹ Suxamethonium provides rapid onset of action and excellent muscular relaxation but is not without side effects. These include changes in intragastric pressure,² unwanted increases in serum potassium in burns patients,³ suxamethonium apnoea,⁴ and postoperative muscle pains.⁵ Suxamethonium itself has a large individual variation in onset of action and time to maximum block so it is not an ideal agent for all patients.

The non-depolarising agents do not provide as rapid an onset of action as suxamethonium. The administration of priming doses of muscle relaxants has not been shown to equal suxamethonium in speed of onset of action,⁶ and this

technique has unpleasant effects on patients and may be dangerous.

We have demonstrated that an induction dose of propofol 2.5 mg/kg provides satisfactory conditions for intubation in 60% of patients. Mild coughing and bucking occurred in 35% of patients and would be unacceptable in certain clinical situations, for example neuroanaesthesia and eye surgery. The ease of laryngoscopy and the short duration of action of propofol make it a useful adjuvant in the assessment of suspected difficult intubation. Muscle pain causes much distress to patients and its absence is advantageous, particularly for day case surgery.

References

1. LEWIS CB. Endotracheal intubation under thiopentone. *Anaesthesia* 1948; 3: 113.
2. ANDERSON N. Changes in intragastric pressure following the administration of suxamethonium. *British Journal of Anaesthesia* 1962; 34: 363.
3. TOHME JD, JOYCE TH, MITCHELL CD. Succinylcholine danger in the burned patient. *Anesthesiology* 1967; 28: 467.
4. HUNTER AR. Suxamethonium apnoea, a study of eighteen cases. *Anaesthesia* 1966; 45: 837.
5. CHURCHILL-DAVIDSON HC. Suxamethonium chloride and muscle pains. *British Journal of Anaesthesia* 1954; 26: 74.
6. GINGOTT N. Relaxants for endotracheal intubation. A useful monitor for time intervals. *Anaesthesia* 1973; 28: 579.

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Propofol for inpatient dental anaesthesia. A comparison of propofol as sole anaesthetic agent with thiopentone and halothane for inpatient dental anaesthesia

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Summary

The induction, maintenance and recovery characteristics of propofol anaesthesia were compared with thiopentone induction and halothane maintenance in 51 spontaneously breathing, intubated patients who underwent dental surgery. Induction with thiopentone produced fewer side effects than propofol, notably pain on injection. Control of the depth of anaesthesia was better in patients who breathed halothane than in those who received intermittent bolus doses of propofol. Recovery characteristics of the two groups were similar.

Key words

Anaesthesia; dental.

Anaesthetics, intravenous; propofol, thiopentone.

The recovery characteristics of propofol are among its most desirable properties. This study was undertaken to see whether propofol can be used as a sole agent in intubated, spontaneously breathing patients during dental surgery. It was compared with a standard technique of thiopentone, nitrous oxide and halothane.

Methods

Fifty-one patients were randomly allocated to receive either propofol alone (25 patients) or thiopentone–halothane as anaesthetic agents for dental surgery. All were of ASA grade 1 except for one epileptic patient in the latter group.

All were inpatients and received premedication with intramuscular papaveretum and hyoscine according to weight, one hour prior to induction. Details are shown in Table 1.

Arterial blood pressure and heart rate were recorded using a Dinamap indirect blood pressure monitor, and the ECG displayed continuously. After baseline recordings, anaesthesia was induced with either propofol 3 mg/kg or thiopentone 4 mg/kg given over 20–30 seconds into a vein on the dorsum of the nondominant hand. Pain on injection and the time to loss of the eyelash reflex were noted, as were any apnoeic episodes. Nasotracheal intubation was facilitated in both groups by intravenous suxamethonium 1 mg/kg. A throat pack was inserted and blood pressure and heart rate again recorded 3 minutes after intubation.

Table 1. Patient data and duration of anaesthesia.

	Propofol (n = 25)	Thiopentone-halothane (n = 26)
Sex, M/F	17/8	15/11
Mean (SD) age, years	23.3 (4.24)	27.1 (SD 8.46)
Mean (SD) weight, kg	68.4 (12.44)	68.4 (SD 11.24)
Anaesthetic duration, minutes	20	21

Ventilation was maintained manually after suxamethonium, using a Bain coaxial system with oxygen in nitrous oxide in a ratio of 1:2 at a fresh gas flow of 70 ml/kg. Halothane was introduced in the thiopentone-halothane group with the onset of spontaneous ventilation. Patients were transferred to the operating theatre where monitoring was re-established. End tidal carbon dioxide (Datex Normo-cap) and halothane concentration (Datex Anaesthetic Agent Monitor) were recorded at 3-minute intervals.

Intermittent doses of propofol (approximately 25% of the induction dose, i.e. 0.75 mg/kg per dose) were administered in the propofol group and heart rate, blood pressure, respiratory pattern and movement were used as the criteria to maintain smooth anaesthesia. Halothane was used in the other group in the lowest concentration necessary to maintain anaesthesia according to the same criteria. Both groups of patients continued to breath oxygen in nitrous oxide in a ratio of 1:2 via a Bain coaxial system with a fresh gas flow of 160 ml/kg.

Nitrous oxide and halothane were discontinued at the end of surgery, the throat pack removed and the oropharynx cleared. The patients' tracheas were extubated and they were transferred to the recovery room where recovery times were noted from the last dose of propofol or from discontinuation of halothane, until patients could open their eyes on command and recall their correct birth date.

Postoperative sequelae were recorded by nursing staff on the ward, and patients were interviewed the following day. Morbidity associated with either technique was noted 24 hours postoperatively.

Statistical analysis. Arterial blood pressure and heart rate

data were subjected to analysis of variance applied at each time point to changes from the baseline. The Wilcoxon rank sum test was applied to the recovery times from the end of the operation and side effects were analysed by the Chi-squared test.

Results

The characteristics of each group and the durations of operation were similar (Table 1).

Induction. Induction was successful in both groups and induction times were similar (Table 2). There were significantly more side effects on induction in the propofol group, especially pain on injection (Table 2). The quality of induction was graded as good or adequate in all patients.

Maintenance. Maintenance doses of propofol were required every 4-15 minutes with a range of 2-10 doses. The mean total dose administered, including the induction dose, was 6.85 mg/kg (SD 1.57) and the mean maintenance dose was 5.84 mg/kg/hour. The mean halothane concentration in the thiopentone-halothane group was 1.3% during the period 2-9 minutes, 1.1% during the period 10-30 minutes and 0.8% after 30 minutes.

There were no statistically significant differences between the groups with respect to systolic blood pressure changes from baseline (Fig. 1). There was a significantly greater increase in diastolic pressure in the thiopentone-halothane group during the period 2-9 minutes ($p = 0.004$). Conversely, there was a significantly greater increase in diastolic pressure in the propofol group during the period 10-30 minutes ($p = 0.029$, Fig. 1). Heart rate was significantly

Table 2. Induction quality and side effects.

	Propofol (n = 25)	Thiopentone-halothane (n = 26)
Mean (SD) Induction time, seconds	36 (8.0)	33 (9.2)
Side effects		
Pain on injection	6	0
Transient flush or rash	4	1
Muscular twitching	1	0
Total	9	1*
Quality of induction		
Good	22	26
Adequate	3	0
Poor	0	0

* $p = 0.005$, significant difference between groups.

Table 3. Control of depth of anaesthesia and side effects during maintenance.

	Propofol (n = 25)	Thiopentone-halothane (n = 26)
Control of anaesthesia		
Good	13	24
Adequate	11	2
Poor	1	0
Side effects		
Coughing	7	4
Transient rash	3	0
Nodal rhythm	1	3
Varying PR interval	0	1
Total	11	8

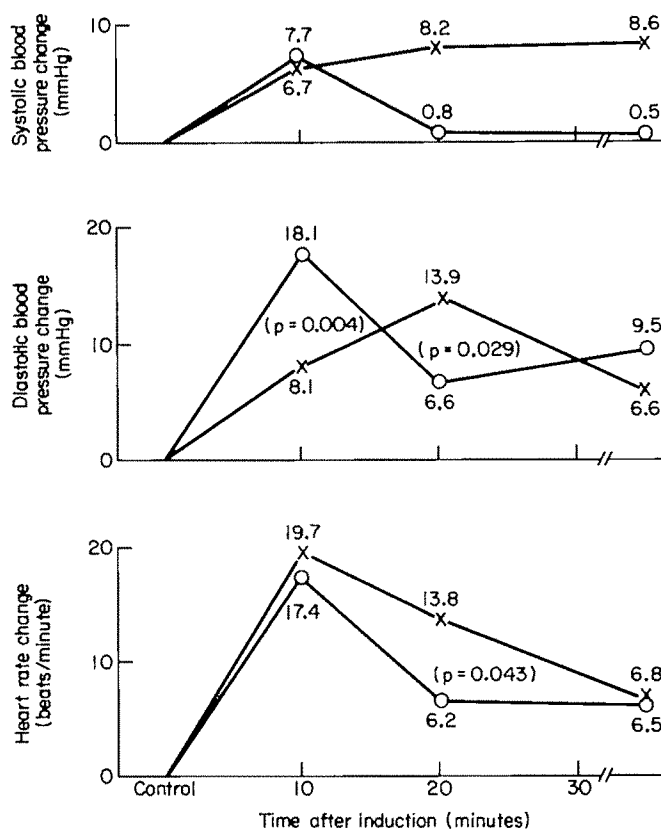


Fig. 1. Changes in systolic and diastolic blood pressure and heart rate from control values after induction with propofol (3 mg/kg) with intermittent propofol maintenance (x), and induction with thiopentone (O) (4 mg/kg) with halothane for maintenance. Points are mean values and p values are given in parentheses for statistically significant differences.

higher in the propofol group during the period 10–30 minutes ($p = 0.043$, Fig. 1). Side effects and dysrhythmias during maintenance were not significantly different (Table 3).

Mean end tidal carbon dioxide tensions were higher in the thiopentone–halothane group throughout anaesthesia: 6.17 kPa at 2–9 minutes, 6.08 kPa at 10–30 minutes and 6.0 kPa after 30 minutes. End tidal carbon dioxide tensions in the propofol group were 5.97, 5.77 and 5.65 kPa, respectively. These differences were not statistically significant.

Control of depth of anaesthesia was judged to be generally better in those who received thiopentone–halothane (Table 3). Slight movement that indicated the need for a supplementary dose of propofol was noted in 16 patients and moderate movement in five. Slight movement occurred in two and moderate movement in one patient given thiopentone–halothane. In no patient was the anaesthetic or surgery abandoned.

Recovery. Recovery times until patients could open their eyes and state their date of birth correctly, were similar in the two groups (Table 4). There were no statistically significant differences between the treatment groups during the early recovery period. One patient who received propofol was nauseated and a second exhibited transient restlessness and confusion.

One patient who was given propofol vomited after 24 hours, while two patients in the thiopentone–halothane

group were nauseated. No venous sequelae were noted in either group and no patient reported perioperative awareness. Postoperative analgesia was required in five members of each group.

Three patients would not choose a propofol anaesthetic again (two due to pain on injection, one due to lethargy). Two patients would not choose thiopentone–halothane again, one due to nausea and a second for an unspecified reason.

Discussion

This study reiterates some of the recognised differences between propofol and the combination of thiopentone induction with halothane maintenance, while it extends our knowledge of propofol as a single agent for anaesthesia by intermittent injection and in dental anaesthesia. An induction dose of propofol 3 mg/kg was selected after a pilot study of 20 patients which used 2.5 mg/kg. The higher dose permitted a smoother transition to spontaneous ventilation after intubation.

Pain on injection of propofol can be reduced by several techniques.^{1,2} The haemodynamic effects of induction have been reported in detail and compared with other agents including thiopentone.^{3–5} However, we noted an increase in heart rate, systolic and diastolic blood pressures after thiopentone and propofol induction and nasotracheal intu-

Table 4. Clinical recovery times.

	Propofol (n = 25)	Thiopentone–halothane (n = 26)
Time to eye opening, minutes	9.6	11.0*
Time to stating birth date, minutes	11.7	14.7†

* $p = 0.438$; † $p = 0.176$.

bation. This may be ascribed to the effect of intubation and the onset of spontaneous ventilation, and is thus an exaggeration of the effect reported by Herregods *et al.*⁶ with intubation and controlled ventilation.

Control of depth of anaesthesia with halothane was regarded as superior to that with intermittent doses of propofol. Blood pressure and heart rate increases during anaesthesia for these stimulating surgical procedures occurred in both groups of patients. Dysrhythmias in both groups required no intervention. The recovery characteristics were similar and confer no advantage on either technique.

The use of techniques to reduce the incidence of pain on injection of propofol, and a propofol infusion^{6,7} rather than intermittent injections for maintenance, may improve the quality of induction and maintenance compared to thiopentone and halothane in spontaneously breathing patients for dental surgery.

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with the permission of the Director General of Medical Services (RAF).

References

1. McCULLOCH MJ, LEES NW. Assessment and modification of pain on induction with propofol ('Diprivan'). *Anaesthesia* 1985; **40**: 1117-20.
2. KAY B, HARGREAVES J, SIVALINGAM T, HEALY TEJ. Intravenous anaesthesia for cystoscopy: a comparison of propofol or methohexitone with alfentanil. *European Journal of Anaesthesiology* 1986; **3**: 111-20.
3. GROUNDS RM, TWIGLEY AJ, CARLI F, WHITWAM JG, MORGAN M. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia* 1985; **40**: 735-40.
4. MACKENZIE N, GRANT IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *British Journal of Anaesthesia* 1985; **57**: 725-31.
5. ROLLY G, VERSICHELEN L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. *Anaesthesia* 1985; **40**: 945-8.
6. HERREGODS L, ROLLY L, VERSICHELEN L, ROSSEEL MT. Propofol combined with nitrous oxide-oxygen for induction and maintenance of anaesthesia. *Anaesthesia* 1987; **42**: 360-5.
7. DE GROOT PMRM, MITSUKURI S, VAN EGMOND J, RUTTEN JMJ, CRUL JF. Comparison of etomidate and propofol for anaesthesia in microlaryngeal surgery. *Anaesthesia* 1987; **42**: 366-72.

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Comparison of a total intravenous anaesthetic technique using a propofol infusion, with an inhalational technique using enflurane for day case surgery

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Summary

A total intravenous anaesthetic technique with a propofol infusion for maintenance of anaesthesia was compared with an inhalational technique that used oxygen, nitrous oxide and enflurane in 98 unpremedicated patients who presented for day case surgery. Overall quality of anaesthesia during induction and maintenance was comparable in both groups. Quality of maintenance of anaesthesia in the propofol group was improved by an increase of the initial infusion rate from 12 to 15 mg/kg/hour. There was a larger decrease in arterial blood pressure after induction in the propofol group but no difference in blood pressure between the groups during maintenance. Recovery times and scores using the Steward scoring system were not significantly different. Nausea and vomiting were slightly less frequent in the propofol group.

Key words

Anaesthesia; outpatient.

Anaesthetics, intravenous; propofol.

Interest in total intravenous anaesthesia has been revived by propofol, the kinetics of which allow both induction and maintenance of anaesthesia with rapid recovery of consciousness. The aim of this study was to compare the quality of induction, maintenance and recovery from anaesthesia between a total intravenous and an inhalational technique in spontaneously breathing, non-intubated patients. An assessment was also made of the infusion rate of propofol required for anaesthesia.

Methods

Ninety-eight unpremedicated female patients who presented for dilatation and curettage or suction termination of pregnancy, aged between 16 and 70 years, were included in the study. Hospital ethical committee approval was obtained and all patients gave informed consent. Patients designated ASA grade 3 or 4, those with previous adverse experience of general anaesthesia or with a history of

atopy or allergy were not studied. Patients were randomly allocated into the two groups.

Propofol group. Intravenous fentanyl 0.1–0.15 mg/kg was given via a cannula placed in the dorsum of the hand, followed one minute later by a dose of propofol titrated to produce anaesthesia. Anaesthesia was maintained with a propofol infusion at a rate altered according to clinical depth of anaesthesia. The infusion was started at a rate of 12 mg/kg/hour once spontaneous ventilation commenced but this was increased to 15 mg/kg/hour later in the study. Bolus doses of propofol were given as required and patients breathed 100% oxygen throughout via a Magill system.

Enflurane group. Intravenous fentanyl 0.1–0.15 mg/kg was followed one minute later by a dose of thiopentone titrated to produce anaesthesia. Anaesthesia was maintained with oxygen 34%, nitrous oxide 66% and a variable concentration of enflurane delivered via a Magill system. Enflurane was started at a concentration of 1.5% which was altered according to clinical depth of anaesthesia.

Anaesthesia was discontinued in both groups after surgery was completed. Arterial blood pressure was monitored prior to induction, at 2 and 5 minutes after induction of anaesthesia and thereafter every 5 minutes using a Datascope Accutorr blood pressure monitor attached to the patient's right arm. Heart rate was measured at the same times with an ECG monitor connected in the CM5 configuration. End tidal carbon dioxide was measured at 2, 5 and 10 minutes after induction of anaesthesia and thereafter every 10 minutes using a Datascope Accucap infrared analyser with gas sampled from the facemask. Conditions were judged to be suitable for surgery when there was adequate jaw relaxation, ocular movement had ceased, pupils were central and breathing was regular and spontaneous. The time that elapsed between induction of anaesthesia and these conditions was recorded. The presence or absence of movement not related to light anaesthesia, twitching, hypertonus, masseter spasm, hiccough, cough and laryngospasm were specifically noted in all patients at induction.

The incidence and duration of apnoea after induction of anaesthesia were recorded. Apnoea of duration longer than 30 seconds was managed by manual intermittent positive pressure ventilation until respiration recommenced. Apnoea that occurred during maintenance of anaesthesia was recorded in addition and if judged to be due to deep anaesthesia, the propofol infusion rate or inspired enflurane concentration was reduced. Light anaesthesia was assessed either by movement in response to surgery or by increased respiratory rate, tachycardia or pupil divergence.

Additional bolus doses of intravenous agent were recorded, as were the durations of surgery and anaesthesia. Recovery times were recorded from the end of anaesthesia until the patients opened their eyes to command and until they were orientated in time and space. Recovery scores were assessed with the Steward scoring system¹ (Table 1)

Table 1. Steward scoring system¹ for assessment of recovery from anaesthesia.

		Score
Wakefulness	Fully awake	2
	Arousable	1
	Not responding	0
Ventilation	Can cough or cry	2
	Breathes easily	1
	Airway requires attention	0
Movement	Moves purposefully	2
	Moves involuntarily	1
	Not moving	0

at 3, 5, 15 and 30 minutes after the end of anaesthesia. The presence or absence of headache, nausea, vomiting, elation/euphoria, depression/crying, confusion, restlessness, and venous phlebitis or thrombosis were also noted prior to discharge to the ward.

Two hours after the end of surgery, patients were asked specifically about awareness during anaesthesia. Any post-operative analgesia administered prior to discharge was recorded.

Results

The groups were similar in respect of age, weight, height, operative and anaesthetic times (Table 2). Induction was

Table 2. Patient details and operative times. Values expressed as mean (SD).

	Propofol (n = 48)	Enflurane (n = 50)
Age, years	31.6 (10.6)	28.9 (13.0)
Weight, kg	64.3 (9.5)	63.1 (12.1)
Height, cm	161.3 (6.2)	160.7 (6.0)
Duration of anaesthesia, minutes	17.5 (6.5)	18.9 (8.1)
Duration of surgery, minutes	6.2 (5.7)	7.7 (7.1)

achieved in all patients with propofol 2.1 mg/kg (SD 0.3) or thiopentone 4.4 mg/kg (SD 0.7). Propofol infusion and utilisation rates during maintenance of anaesthesia are shown in Table 3. The mean inspired enflurane concentration during maintenance of anaesthesia was 1.8% (SD 0.9%).

Table 3. Mean (SD) dosages, utilisation and infusion rates of propofol.

Induction dose, mg/kg	2.1 (0.3)
Total maintenance dose, mg/kg	2.6 (1.1)
Overall duration of anaesthesia, minutes	17.5 (6.5)
Mean rate of utilisation during maintenance, mg/kg/hour	9.2 (2.9)
Mean rate of utilisation during induction and maintenance, mg/kg/hour	17.2 (4.4)
Initial infusion rate, mg/kg/hour	12.8 (2.0)
Steady-state infusion rate, mg/kg/hour	11.5 (3.0)

Apnoea at induction was the most significant feature in both groups and it lasted longer than 30 seconds in 49% of the propofol group and 54% of the enflurane group. The overall duration of apnoea was significantly longer in the propofol group (161 seconds, SD 191) than in the enflurane group (90 seconds, SD 123; $p = 0.05$).

Patients were ready for surgery sooner in the propofol group than in the enflurane group. Twenty-five out of 48 patients given propofol were ready for surgery in less than 3 minutes, compared with 16 out of 50 who received enflurane ($p = 0.05$). There was a significant but transient decrease in arterial systolic and diastolic blood pressures from pre-anaesthetic values in both groups in the period 2–9 minutes after induction. However, there was a significantly larger decrease in both systolic ($p = 0.016$) and diastolic ($p = 0.002$) blood pressures in the propofol group (Table 4). There was no significant difference in arterial pressure between the two groups in the period 10–30 minutes after induction and there was no significant change in heart rate from baseline levels in either group (Table 4). End tidal carbon dioxide concentration was similar in both groups at all times during the maintenance of anaesthesia and remained in the normal range (Table 4).

The incidence of side effects during maintenance of anaesthesia was similar in both groups and there was no significant difference in periods of light or deep anaesthesia

Table 4. Mean (SD) cardiovascular parameters and end tidal carbon dioxide tensions.

	Baseline		2–9 minutes		10–30 minutes	
	Propofol	Enflurane	Propofol	Enflurane	Propofol	Enflurane
Systolic arterial pressure, mmHg	120.9 (17.8)	119.0 (17.1)	105.0 (14.7)*‡	109.0 (16.3)*	114.0 (16.4)	109.6 (18.6)
Diastolic arterial pressure, mmHg	69.0 (13.6)	68.0 (12.6)	57.1 (10.4)*§	62.3 (11.5)†	61.6 (12.0)	63.3 (13.6)
Heart rate, beats/minute	79.8 (11.6)	80.4 (14.7)	75.9 (10.6)	78.8 (9.6)	76.4 (11.6)	81.5 (14.2)
PE _T CO ₂			4.75 (0.67)	4.91 (0.53)	4.90 (0.99)	5.28 (0.81)

* $p = 0.001$, † $p = 0.05$, significant changes from baseline; ‡ $p = 0.016$, § $p = 0.02$, significant differences between groups.

between the two. Additional boluses of propofol were required to maintain anaesthesia in 12 of the initial 28 patients in the propofol group. The initial infusion rate of propofol was therefore increased from 12 to 15 mg/kg/hour in an attempt to decrease the incidence of light anaesthesia and the need to give bolus doses. Periods of light anaesthesia were reduced from 53% to 23% by the increase in infusion rate ($p < 0.05$) and the need for additional boluses was reduced from 43% to 23% ($p < 0.1$). Periods of deep anaesthesia with apnoea were similar at both infusion rates and occurred in 9.5% of patients at the higher, and 3.6% of patients at the lower initial infusion rate. Periods of light anaesthesia were recorded in 42% and deep anaesthesia in 6% of the patients in the enflurane group.

There were no significant differences in recovery times. Eyes were open at an average of 4.6 minutes in the propofol group compared with 5.1 minutes in those given enflurane. Patients were orientated at a mean of 6.6 minutes after propofol and 8.0 minutes after enflurane. Recovery room scores at 3 and 5 minutes were not significantly different. However, all patients in the propofol group achieved a maximum Steward score at 15 minutes whereas five out of 50 in the enflurane group had not reached full recovery on Steward scoring ($p = 0.05$). All patients were fully awake with a maximum Steward score at 30 minutes. There was no difference in postoperative analgesic requirements between the two groups.

There was a significantly lower incidence of both nausea and vomiting in the postoperative period among those who received propofol. Nausea was recorded in 2% of these patients compared to 21% of those given enflurane ($p < 0.001$). Vomiting was absent after propofol but occurred in 12.5% of the enflurane group ($p < 0.001$). Awareness was not elicited from any patient in the study.

Discussion

Total intravenous anaesthesia has many potential advantages over inhalational anaesthesia. Nitrous oxide is contraindicated in certain anaesthetic situations; indeed, some authorities consider that nitrous oxide should be used only when it is specifically indicated.² Volatile agents also have both specific and general side effects which can be avoided by their omission from the general anaesthetic technique. The omission of nitrous oxide and volatile agents from anaesthesia also solves the problem of gaseous operating theatre pollution.

Infusion rather than intermittent bolus administration of intravenous anaesthetics is the logical choice if smooth anaesthesia is to be obtained. Technically, total intravenous anaesthesia using infusions might appear to be more complex than inhalational anaesthesia. Extra time is required for initial preparation of the infusion system; once set up, it proved reliable and easy to use. Total intravenous techniques have the advantage that the depth of anaesthesia can be increased more rapidly, by increasing the infusion rate or giving bolus doses of the anaesthetic agent, whereas inhalational anaesthesia relies on continuous spontaneous ventilation to increase the alveolar concentration of the anaesthetic agent. The greater number of patients ready for

surgery in less than 3 minutes is probably a reflection of this.

It was found in practice that an infusion rate of 15 mg/kg/hour, which was decreased after surgery commenced, produced smoother anaesthesia than an initial rate of 12 mg/kg/hour. The initial infusion rate is higher than that recommended in some other studies in spontaneously breathing patients.^{3,4} This is possibly because of the type of surgery; the surgical stimulus of dilatation of the cervix is stronger than that of many other procedures. Studies which suggest initial infusion rates of 12 mg/kg/hour also incorporated nitrous oxide in the anaesthetic technique.

Significant decreases in arterial pressures from baseline levels are known to occur with propofol⁴ and our study confirms this. There was an initial large decrease in blood pressure in the propofol group but spontaneous recovery occurred and there was no difference between the propofol and enflurane groups in short-term maintenance of anaesthesia. This technique is therefore suitable for all patients except those in whom cardiovascular stability is a major consideration.

Apnoea on induction of duration more than 30 seconds was equally common in both groups. The duration was longer in the propofol group but apnoea was easily managed by manual intermittent positive pressure ventilation. The incidence of apnoea in the propofol group in this study is approximately half that in another study which used a similar technique.⁵ Spontaneous ventilation recommenced at normocapnic levels and normocapnia was maintained in all patients studied. It is possible that apnoea may be further reduced by the use of smaller incremental doses or infusions of opioid.

Recovery times were shorter, but not significantly so, in the propofol group. Recovery scores after propofol were significantly better only at 15 minutes after the end of anaesthesia. Patients given propofol showed better recovery than those given enflurane, several of whom were still drowsy 2–4 hours after surgery. All patients in the propofol group were fully awake by this time. This difference was not detected by the Steward scoring system but more sensitive techniques for the assessment of postoperative recovery might have supported this clinical impression.

The low incidence of nausea and vomiting in the propofol group is consistent with other studies that used propofol for induction and maintenance of anaesthesia.⁵ The omission of nitrous oxide may contribute to this finding^{6,7} and it is also possible that propofol has intrinsic antiemetic properties.^{8,9} This makes the technique particularly suitable for day case anaesthesia. Modifications of this technique may also serve to limit nausea and vomiting in the early postoperative period in fields such as neuroanaesthesia and ophthalmic anaesthesia, where it may compromise completed surgery.

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References

1. STEWARD DJ. A simplified scoring system for the post-operative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-3.
2. EGER EI II. Should we use nitrous oxide? In: EGER EI II, ed. *Nitrous oxide*. New York: Elsevier Science Publishing Company, Inc., 1985: 339-43.
3. MAJOR E, VERNIQUET AJW, YATE PM, WADDELL TK. Disopropofol and fentanyl for total intravenous anaesthesia. *Anaesthesia* 1982; **37**: 541-7.
4. PATRICK MR, BLAIR LJ, FENEK RO, SEBEL PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 23-7.
5. MCLEOD B, BOHEIMER N. Propofol ('Diprivan') infusion as main agent for day case surgery. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 105-7.
6. LONIE DS, HARPER NJN. Nitrous oxide anaesthesia and vomiting. *Anaesthesia* 1986; **41**: 703-7.
7. ALEXANDER GD, SKUPSKI JN, BROWN EM. The role of nitrous oxide in postoperative nausea and vomiting. *Anesthesia and Analgesia* 1984; **63**: 175.
8. MCCOLLUM JSC, MILLIGAN KR, DUNDEE JW. Has propofol an anti-emetic action? *British Journal of Anaesthesia* 1987; **59**: 654P.
9. MILLIGAN KR, MCCOLLUM JSC, DUNDEE JW. An investigation into the anti-emetic effect of propofol. *British Journal of Clinical Pharmacology* 1987; **23**: 608P-9P.

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Comparison between propofol and midazolam as sedative agents for surgery under regional anaesthesia

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Summary

Propofol (25 patients) or midazolam (25 patients) was used to provide sedation in patients who underwent abdominal or orthopaedic surgery under epidural anaesthesia after intravenous premedication with droperidol 1 mg and fentanyl 20 µg. The quality of sedation whilst the block was performed, was assessed as good in 19 patients after propofol 1.49 mg/kg but six patients exhibited uncontrolled movement. Good sedation was provided in 22 patients after midazolam 3 mg. A mean infusion rate of propofol of 1.74 mg/kg/hour resulted in easily controllable sedation during the procedure. Eleven patients given midazolam required no further sedation but a mean of 5.79 mg was needed in the remaining 14 patients; the dose was unpredictable in individual patients. Recovery was significantly more rapid in the propofol group.

Key words

*Anaesthetics, intravenous; propofol.
Hypnotics, benzodiazepines; midazolam.*

Regional anaesthesia has many advantages over general anaesthesia and is associated with a lower incidence of deep vein thrombosis and pulmonary embolism postoperatively,¹ minimal effects on respiratory function²⁻⁵ and no change in cerebral function in the elderly if hypotension is avoided.⁶ For these reasons, 84% of abdominal, orthopaedic, gynaecological, urological and cosmetic surgery in this institution is performed under regional anaesthesia.

Most patients, however, prefer to have no memory of the surgical procedure and some form of sedation is therefore necessary. We have for more than 10 years used a combination of a neuroleptic (droperidol), an opioid (fentanyl) and a benzodiazepine (initially flunitrazepam but more recently midazolam) for this purpose; all are given just before the epidural block is performed. The aim of this open, randomised study, was to compare the effects of midazolam with those of propofol when given in combination with droperidol and fentanyl.

Methods

Fifty patients of ASA grade 1 or 2, aged 17-60 years and scheduled to undergo abdominal or orthopaedic surgery under epidural analgesia, were randomly allocated into two equal groups (Table 1). They were given droperidol 1 mg and fentanyl 20 µg into a forearm vein on arrival in the

Table 1. Demographic characteristics of patients. Values expressed as mean (SEM) or number of patients, as appropriate.

	Group 1 (propofol) (n = 25)	Group 2 (midazolam) (n = 25)
Sex ratio, M/F	12/13	12/13
Age, years	35.08 (3.18)	39.56 (2.43)
Weight, kg	65.88 (2.32)	69.48 (2.46)
Height, cm	168.56 (2.27)	170.24 (1.33)
ASA grade 1/grade 2	23/2	23/2
Surgery, orthopaedic/abdominal	23/2	18/7
Duration of procedure*, minutes	130.7 (12.8)	143.8 (10.0)

* From start of induction to end of surgery.

anaesthetic room. The patients of group 1 were given an infusion of propofol 1.49 mg/kg 10 minutes later, at a rate of 80 mg/minute while group 2 patients received a 50 µg/kg bolus of midazolam. An epidural was performed when sedation was satisfactory, using 0.5% or 0.75% bupivacaine with adrenaline together with either fentanyl or sufentanil. Sedation in group 1 was maintained with a continuous infusion of propofol 1.5-3.0 mg/kg/hour which was discontinued at the end of surgery. Additional boluses of midazolam 1.5-3.0 mg were given when required in group 2.

Heart rate, arterial blood pressure, oxygen saturation and conscious level were assessed before and after droperidol

and fentanyl, immediately after propofol or midazolam, 2 minutes and 5 minutes after these drugs and at 5-minute intervals thereafter. The time to awakening was noted and the quality of recovery evaluated using the Steward score.⁷ Patients were asked 2 and 24 hours after surgery if they could recognise two pictures, one shown before and one shown 10 minutes after induction, in order to assess amnesia.

Results

Induction. The quality of sedation whilst the block was performed, was assessed as good in 19 patients given propofol but six patients exhibited uncontrolled movements (Table 2). These patients were too deeply sedated and were in fact

Table 2. Induction data.

	Group 1 (propofol) (n = 25)	Group 2 (midazolam) (n = 25)
Induction dose (mg/kg)	1.49	0.05
Quality of sedation		
Good	19 (76%)	22 (88%)
Adequate	1 (4%)	3 (12%)
Insufficient*	5 (20%)	0
Loss of eyelash reflex	17 (68%)	2 (8%)
Systolic blood pressure change	-21.37% †	-21.36% †
Mean blood pressure change	-20.65% †	-19.55% †
Diastolic blood pressure change	-19.98% †	-17.96% †
Heart rate change	-2.85%	-2.27%
Apnoea	2 (8%)	0
Oxygen saturation change	-4.00% †	-2.67% †
Side effects	9 (36%)	2 (8%)

* Too deep or movements.

† $p < 0.001$ compared with baseline (two-tailed paired Student's *t*-test).

lightly anaesthetised, with absent eyelash reflexes, and this prevented cooperation. Sedation was assessed as good in 22 of the midazolam patients at this time; the patients appeared to be asleep but the eyelash reflex was preserved and they were able to obey commands.

Heart rate remained almost unchanged in the two groups but there was a significant, although transient decrease in arterial blood pressure after both drugs. However, the baseline values were somewhat elevated, probably because

no premedication was given. Two patients became apnoeic after propofol and there was a mean decrease in oxygen saturation at 4% compared to 2.67% in the midazolam group, none of whom became apnoeic. Respiratory obstruction occurred in one patient who received propofol. One patient after midazolam sweated profusely but this stopped spontaneously, while another had marked and prolonged shivering despite additional doses of midazolam. Two patients complained of mild pain during injection of propofol.

Maintenance. The mean infusion rate in the propofol group was 1.74 mg/kg/hour and the level of sedation was easily controlled by manipulation of the rate (Table 3). Eleven patients in the midazolam group did not require additional sedation. The remaining 14 patients required a mean of 5.79 mg but the dose required was not predictable; there was no correlation with age, weight or duration of the procedure. There was a much wider variation in the midazolam group in respect of the total dose of drug.

The haemodynamic changes during maintenance are related to sympathetic block rather than to degree of sedation. Similarly, shivering can also be related to epidural block, although the incidence was greater in those who received propofol (36% compared to 16%). Oxygen saturation during maintenance returned almost to baseline values.

Recovery. Recovery was significantly more rapid in the propofol group than in those given midazolam. Steward's score after 15 minutes was maximal in 24 of the former patients, compared to 18 of the latter ($p = 0.02$, Chi-squared test). Six patients who received midazolam had still not achieved a maximum score 2 hours after surgery. There was no difference in the incidence of amnesia (60% after propofol and 56% after midazolam).

Discussion

There are several methods of sedation during regional anaesthesia. The oral and intramuscular routes often result in inadequate levels of sedation; light general anaesthesia ensures light sleep and rapid recovery but the attendant risks must be taken into account. The intravenous route with the appropriate drug in low doses, offers a controllable means of sedation, with rapid onset and recovery. Both propofol and midazolam provided good sedation after intravenous premedication with droperidol and fentanyl, and all patients would have the same drugs again. Our findings

Table 3. Maintenance data.

	Group 1 (propofol) (n = 25)	Group 2 (midazolam) (n = 25)
Dose		
Mean (SD)	1.74 mg/kg/hour (0.58)	5.79 mg (4.40) (n = 14)*
Range	1-3 mg/kg/hour	1.5-15 mg
Total consumption		
Mean (SD)	2.65 mg/kg/hour (0.88)	42 µg/kg/hour (0.034)
Range	0.81-4.35 mg/kg/hour	12-145 µg/kg/hour
Quality of sedation		
Desirable	22 (88%)	19 (76%)
Too deep	1 (4%)	1 (4%)
Inadequate	2 (8%)	5 (20%)
Cardiovascular changes in relation to regional anaesthesia		
Oxygen saturation change	-1%	-0.84%
Side effects (shivering)	9 (36%)	4 (16%)

* Eleven patients in the midazolam group received no increments.

confirm those of others with regard to the rapid recovery after propofol⁸⁻¹⁰ and possible delayed recovery after midazolam.^{11,12}

The haemodynamic and respiratory changes were acceptable in our patients, although care must be taken in the elderly and high risk patients. Side effects were rare, apart from shivering, which was commoner after propofol and always ceased when the infusion was stopped.

Further studies are required to find the optimum dose of propofol and midazolam to provide sedation for patients during regional anaesthesia.

References

1. MODIG J, BORG T, KARLSTRÖM G, MARIPUU E, SAHLSTEDT B. Thromboembolism after total hip replacement: role of epidural and general anaesthesia. *Anesthesia and Analgesia* 1983; **62**: 174-80.
2. FREUND FG, BONICA JJ, WARD RJ, AKAMATSU TJ, KENNEDY WF Jr. Ventilatory reserve and level of motor block during high spinal and epidural anaesthesia. *Anesthesiology* 1967; **28**: 834-7.
3. SJÖGREN S, WRIGHT B. Respiratory changes during continuous epidural blockade. *Acta Anaesthesiologica Scandinavica* 1972; **16**: 27-49.
4. WAHBA WM, CRAIG DB. The cardiorespiratory effects of thoracic epidural anaesthesia. *Canadian Anaesthetists' Society Journal* 1972; **19**: 8-19.
5. MANKIKIAN B, CANTINEAU JP, SARTENE R, DERIAZ H, CLERGUE F, VIARS P. Improvement of diaphragmatic function by a thoracic extradural block after upper abdominal surgery. *Anesthesiology* 1985; **63**: A516.
6. MAURETTE P, CASTAGNERA L, VIVIER C, ERNY P. Comparison of psychological function in the elderly after spinal or general anaesthesia. *MAPAR. VIIth Annual Meeting of the European Society of Regional Anaesthesia*.
7. STEWARD DJ. A simplified scoring system for the postoperative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-3.
8. GEPTS E, CLAEYS MA, CAMU F, SMEKENS L. Infusion of propofol ('Diprivan') as sedative technique for colonoscopies. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 120-6.
9. JESSOP E, GROUNDS RM, MORGAN M, LUMLEY J. Comparison of infusions of propofol and methohexitone to provide light general anaesthesia during surgery with regional blockade. *British Journal of Anaesthesia* 1985; **57**: 1173-7.
10. MACKENZIE N, GRANT IS. Propofol for intravenous sedation. *Anaesthesia* 1987; **42**: 3-6.
11. GAMBLE JAS, KAWAR P, DUNDEE JW, MOORE JW, BRIGGS LP. Evaluation of midazolam as an intravenous induction agent. *Anaesthesia* 1981; **36**: 868-73.
12. HARPER KW, COLLIER PS, DUNDEE JW, ELLIOTT P, HALLIDAY NJ, LOWRY KG. Age and nature of operation influence the pharmacokinetics of midazolam. *British Journal of Anaesthesia* 1985; **57**: 866-71.

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Recovery times and side effects after propofol infusion and after isoflurane during ear surgery with additional infiltration anaesthesia

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Summary

Two anaesthetic procedures that did not include nitrous oxide were compared in a randomised study of 50 patients for tympanoplasty and tympanoscopy: propofol given for induction and maintenance, and thiopentone-isoflurane given for induction and maintenance, respectively. Induction in the first group was with a bolus injection of propofol and the same agent was given for the duration of anaesthesia by continuous intravenous administration. Thiopentone was given until loss of the eyelash reflex and anaesthesia maintained with isoflurane 0.4-2.0%. Analgesia was achieved in both groups by fentanyl given intravenously and by local injection of mepivacaine with ornipressin. The two patient groups were analysed for age, sex and weight as well as for side effects during the induction, maintenance and recovery periods, such as coughing, vomiting, venous pain, spontaneous movements, singultus, headaches, dysrhythmias and psychic disorders possibly due to anaesthesia. Side effects were moderate in both groups. Recovery time was statistically significantly shorter in the propofol group and the patients in this group appeared to be much more aware after recovery than those in the thiopentone-isoflurane group.

Key words

*Anaesthetics, intravenous; propofol.
Anaesthetics, volatile; isoflurane.*

A large amount of information has been collected about this intravenous anaesthetic drug in general surgery and gynaecology.¹⁻³ However, little experience has been obtained in ENT surgery⁴ and nearly all studies have used a combination of propofol and nitrous oxide in their anaesthetic procedure.

The purpose of this study was to evaluate the possible benefits and disadvantages of propofol as an anaesthetic drug for tympanoplasty and tympanoscopy. The procedure with propofol involved no other narcotic drug and was compared with a thiopentone-isoflurane procedure that did not include nitrous oxide.

Patients and methods

Fifty patients classified as ASA grade 1-3, aged between 16 and 77 years and scheduled for tympanoplasty or tympanoscopy, were studied. All patients gave informed consent before they participated in the study which was approved by the hospital ethical committee.

Patients were premedicated with atropine 0.5 mg, promethazine 50 mg and pethidine 1 mg/kg intramuscularly given 30-45 minutes before induction of anaesthesia. A plastic cannula was inserted in a large vein of the hand or forearm upon arrival in the operating theatre, and connected to an infusion of a crystalloid solution. The electro-

cardiogram was monitored continuously and arterial blood pressure recorded intermittently with an automatic non-invasive blood pressure monitor (Dinamap) at 5-minute intervals. Pancuronium 1–2 mg, droperidol 2.5 mg and fentanyl 0.1–0.2 mg were given intravenously to all patients before induction of anaesthesia. Suxamethonium was given to facilitate tracheal intubation and all patients received mechanical ventilation of the lungs with 65% air and 35% oxygen. Analgesia was provided by local injection of 0.5% mepivacaine with ornipressin and further bolus doses of fentanyl 0.1 mg when signs of painful reaction to surgical stimuli occurred. Controlled hypotension was instituted with nitroglycerine if necessary, in order to keep local bleeding to a minimum.

Patients were allocated randomly to two groups of 25 each. Propofol was used for induction of anaesthesia in group 1; the individual dosage was increased until the eyelash reflex was lost. Anaesthesia was maintained with a continuous controlled infusion of the same agent immediately following induction. The initial rate of 0.2 mg/kg/minute was reduced after 10 minutes to 0.1 mg/kg/minute. The infusion was stopped at the end of surgery.

Anaesthesia in group 2 was induced with a dose of thiopentone titrated in the same way as in group 1. Isoflurane 0.4–2.0% was administered for maintenance. Stability and depth of anaesthesia were evaluated with regard to the lack of, or need for, additional bolus doses of the hypnotic agent and of fentanyl. Possible drug-related side effects were recorded for both groups from induction of anaesthesia until 24 hours postoperatively. The intensity of pain on injection of the intravenous anaesthetics was assessed as mild (minor sensation), moderate (discomfort admitted on request) or severe (spontaneous indication of pain).

Recovery from anaesthesia was assessed by the patient's ability to open eyes on command, to show their tongue on command and to recall date of birth. Statistical evaluation of these three variables was done with the Wilcoxon test.

Results

The two groups were comparable for sex, age, weight and duration of anaesthesia (Table 1). Anaesthesia was induced

Table 1. Patient data and duration of anaesthesia in two randomised groups. Values expressed as mean (SD)

	Propofol (n = 25)	Thiopentone- isoflurane (n = 25)
Sex, M/F	13/12	15/10
Age, years	41.2 (13.9)	46.1 (14.5)
Weight, kg	70.4 (12.9)	71.2 (10.6)
Duration of anaesthesia, minutes	109.8 (63.4)	121.7 (52.3)

with a mean (SD) dose of 2.16 (0.38) mg/kg propofol in group 1 and with 4.52 (0.42) mg/kg thiopentone in group 2. The induction time (from start of injection until loss of eyelash reflex) was 63.0 (29.80) seconds in the propofol group and 73.2 (54.94) seconds in the thiopentone group. Apnoea was observed in all patients after administration of the induction dose. Measurement of the duration of apnoea was not relevant since suxamethonium was given. Induction was smooth in both groups. Coldness on injection was noticed by one patient in the thiopentone group; tingling occurred in one patient in the propofol group and mild venous pain in two. One patient in the thiopentone group showed spontaneous movement, one had hiccough and one, cough; these were not observed in the propofol group (Table 2).

Table 2. Side effects during induction

	Propofol (n = 25)	Thiopentone- isoflurane (n = 25)
Venous pain on injection		
Mild	2	0
Moderate	0	0
Severe	0	0
Coldness or tingling	1	1
Spontaneous movement	0	1
Hiccough	0	1
Cough	0	1

Table 3. Side effects during maintenance.

	Propofol (n = 25)	Thiopentone-isoflurane (n = 25)
Spontaneous movement	3	3
Bradycardia	0	3
Hiccough	0	1
Cough	0	4

Side effects during maintenance of anaesthesia are shown in Table 3 and occurred more often in the thiopentone-isoflurane group. The total dosage of fentanyl given for analgesia (induction plus additional doses) was nearly the same in both groups, approximately 0.04 µg/kg/minute. The level of anaesthesia varied in both groups but was easily controlled. Four patients who received propofol and nine patients in the thiopentone-isoflurane group needed a further bolus of the respective hypnotic agent. Recovery time was short in both groups but was statistically shorter with propofol (Table 4). Furthermore, the patients in the

Table 4. Recovery times. Values expressed as median (range).

Time in minutes to:	Propofol (n = 25)	Thiopentone- isoflurane (n = 25)
Open eyes on command	10.0 (0.0–30.0)	15.0 (3.0–45.0)*
Show tongue	15.0 (0.0–35.0)	20.0 (3.0–65.0)†
Recall date of birth	18.0 (5.0–40.0)	25.0 (7.0–80.0)†

* p = 0.02, † p = 0.04, significant differences between groups

propofol group generally appeared to be much more aware after recovery than those in the thiopentone-isoflurane group.

Side effects observed during recovery were coughing (seven patients in group 1 and 10 patients in group 2) and confusion for about 10 minutes in one patient from the propofol group. No other side effects were observed (Table 5). All patients were content with their anaesthetic on questioning and no patient recalled any events during anaesthesia and surgery; none showed any venous sequelae in the postoperative period.

Discussion

It is widely accepted that only general anaesthesia can provide the optimal operating conditions required in middle

Table 5. Side effects during recovery

	Propofol (n = 25)	Thiopentone-isoflurane (n = 25)
Cough	7	10
Confusion	1	0
Vomiting	0	0
Headache	0	0

ear microsurgery. An absolute lack of spontaneous movement of the patient and, in many cases, controlled hypotension for minimal bleeding are of paramount importance. However, the use of nitrous oxide in tympanoplasty is not desirable because of its diffusion properties which increase the gas pressure in the closed middle ear spaces and thus endanger the correct placement of the autograft. General anaesthesia without nitrous oxide is therefore desirable.

A continuous infusion of propofol, as described here, effectively produced stable anaesthesia without the use of nitrous oxide. The dosage of propofol needed for induction was low compared with other studies.^{2,5,6} Premedication does not influence the induction dosage⁷⁻¹⁰ so this is presumably due to the dose of fentanyl given shortly before induction.

Anaesthesia with a continuous infusion of propofol was easier to maintain at a steady level compared with thiopentone-isoflurane, since additional bolus injections were necessary considerably less often. This was true even for prolonged anaesthesia (Table 1); most other studies have considered propofol in procedures of shorter duration.^{5,11}

Side effects were moderate during induction and maintenance of anaesthesia (Tables 2 and 3). The low incidence of venous pain on injection of propofol, contrary to earlier studies,^{3,6} may be attributed to the slow injection technique. Coughing during induction and maintenance occurred markedly less often in the propofol group and this may indicate a suppressive effect of this drug on laryngeal reflexes.¹²

We found short recovery times after propofol in agreement with other authors,^{3,4,10} even after prolonged anaesthetic procedures. Recovery time in the propofol group was significantly shorter than in the control group and quality of recovery was better. This may be attributed partly to the fact that the isoflurane concentration had to be increased approximately twofold in order to compensate for the absence of nitrous oxide.

In conclusion, propofol infusion without nitrous oxide inhalation proved to be an effective and safe general anaesthetic procedure in middle ear surgery; nitrous oxide was easily replaceable by local analgesia and small doses of fentanyl, and tissue grafting in tympanoplasty was thereby facilitated.

Acknowledgments

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References

1. KAY B, ROLLY G. ICI 35868, a new intravenous induction agent. *Acta Anaesthesiologica Belgica* 1977; **28**: 303.
2. KAY NH, UPPINGTON J, SEAR JW, ALLEN MC. Use of an emulsion of ICI 35868 (propofol) for the induction and maintenance of anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 736-42.
3. WALMSLEY AJ, McLEOD B, PONTE J. The new formulation of ICI 35868 (propofol) as the main agent for minor surgical procedures. *European Journal of Anaesthesiology* 1986; **3**: 19-26.
4. HERREGODS L, ROLLY G, VERSICHELEN L, ROSSEEL MT. Propofol combined with nitrous oxide-oxygen for induction and maintenance of anaesthesia. *Anaesthesia* 1987; **42**: 360-5.
5. MACKENZIE N, GRANT IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *British Journal of Anaesthesia* 1985; **57**: 725-31.
6. NIGHTINGALE P, HEALY TEJ, HARGREAVES J, MCGUINNESS K, KAY B. Propofol in emulsion form: induction characteristics and venous sequelae. *British Journal of Anaesthesia* 1984; **56**: 808P.
7. BRIGGS LP, BAHAR M, BEERS HTB, CLARKE RSJ, DUNDEE JW, WRIGHT PJ, MCAULEY DM, O'NEIL MP. Effect of pre-anaesthetic medication on anaesthesia with ICI 35868. *British Journal of Anaesthesia* 1982; **54**: 303-6.
8. FRAGEN RJ, DEGROOD PM, ROBERTSON EN, BOOIJ LDHJ, CRUL JF. Effects of premedication on Diprivan induction. *British Journal of Anaesthesia* 1982; **54**: 913-6.
9. ROLLY G, VERSICHELEN L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. *Anaesthesia* 1985; **40**: 945-8.
10. TURTLE MJ, CULLEN P, PRYS-ROBERTS C, COATES D, MONK CR, FAROQUI MH. Dose requirements of propofol by infusion during nitrous oxide anaesthesia in man. II. Patients premedicated with lorazepam. *British Journal of Anaesthesia* 1987; **59**: 283-7.
11. DE GROOD PMRM, MITSUKURI S, VAN EGMOND J, RUTTEN JMJ, CRUL JF. Comparison of etomidate and propofol for anaesthesia in microlaryngeal surgery. *Anaesthesia* 1987; **42**: 366-72.
12. DEGROOD PMRM, VAN EGMOND J, VAN DER WETERING M, VAN BEEM HB, BOOIJ LDHJ, CRUL JF. Lack of effects of emulsified propofol (Diprivan) on vecuronium pharmacodynamics—preliminary results in man. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 28-30.

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A comparison of propofol and midazolam by infusion to provide sedation in patients who receive spinal anaesthesia

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Summary

Twenty patients scheduled for orthopaedic surgery under spinal anaesthesia received by intravenous infusion either 1% propofol or 0.1% midazolam at a rate adjusted to maintain adequate sedation as judged on a five-point scale. No other anaesthetic or analgesic drugs were given. The mean time to reach the required level of sedation was similar in both groups and the quality and ease of control of sedation were good in all patients. Mean infusion rates were 3.73 mg/kg/hour for propofol and 0.27 mg/kg/hour for midazolam. Airway maintenance was excellent and there were no side effects other than restlessness of the arms in one patient in each group. Recovery, judged by ability to open the eyes and recall date of birth, was significantly more rapid after propofol than after midazolam (2 and 10 minutes respectively after the end of infusion) and two patients in the latter group were

unduly drowsy in the initial postoperative period. Pre- and postoperative amnesia were greater in the midazolam group but no patient had recall of peri-operative events. Psychometric tests showed significantly better recovery of higher mental function after propofol for up to 2 hours after surgery.

Key words

Anaesthetics, intravenous; propofol.
Hypnotics, benzodiazepines; midazolam.

Propofol infusion was found to provide excellent sedation during spinal anaesthesia in a previous open study.¹ The present study compared propofol with a standard sedative agent (midazolam) when used in this manner.

Methods

Twenty patients of ASA grade 1 or 2 over the age of 16 years and scheduled to undergo orthopaedic surgery under spinal anaesthesia were studied. Patients were randomly assigned to receive either propofol or midazolam.

Baseline psychometric measurements of critical flicker fusion threshold (CFFT) and choice reaction time (CRT) were made using the Leeds psychomotor tester² before operation. All patients were premedicated with temazepam 10–20 mg orally 1–2 hours prior to the procedure.

An intravenous infusion of Hartmann's solution was started on arrival in the anaesthetic room and baseline heart rate and arterial blood pressure recorded. An infusion of 1% propofol or 0.1% midazolam was started via syringe pump into the intravenous line at this time. Spinal anaesthesia was established by an intrathecal injection of 2.5–3.0 ml plain bupivacaine 0.75% through a 25-gauge spinal needle.

The propofol infusion was started at 6 mg/kg/hour and reduced to 4 mg/kg/hour after 10 minutes. The midazolam

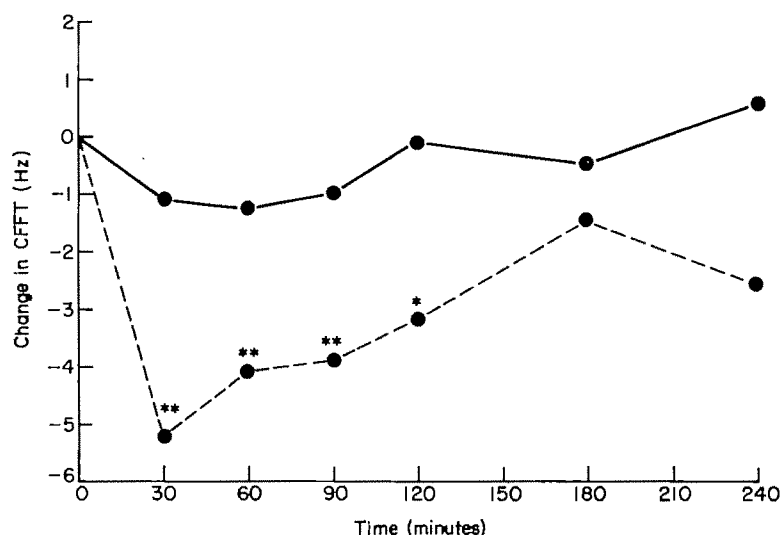


Fig. 1. Mean changes from pre-operative baseline of CFFT. ---, Midazolam; —, propofol. * $p < 0.01$, ** $p < 0.005$.

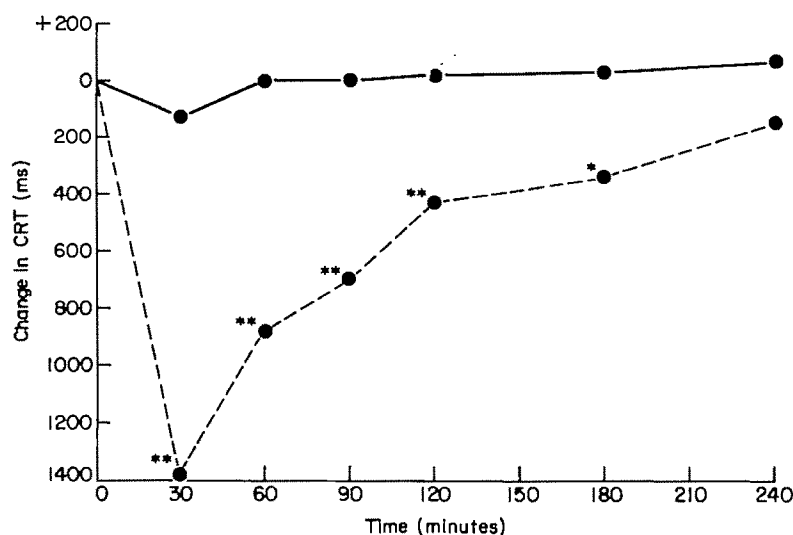


Fig. 2. Mean changes from pre-operative baseline of CRT. Values higher on the ordinate indicate improvement. ---, Midazolam; —, propofol. * $p < 0.01$, ** $p < 0.005$.

infusion was started at 0.5 mg/kg/hour (after an exploratory dose-finding study). The infusion rates were adjusted thereafter to maintain an appropriate level of sedation (level 4) on a five-point sedation scale (Table 1).

Table 1. Sedation scores

Score	Degree of sedation
1	Fully awake and orientated
2	Drowsy
3	Eyes closed but rousable to command
4	Eyes closed but rousable to mild physical stimulation (earlobe tug)
5	Eyes closed but unrousable to mild physical stimulation

The times to reach each stage of sedation were noted. Conscious level, heart rate and arterial blood pressure were assessed at 5-minute intervals for the first 30 minutes and at 10-minute intervals thereafter. All patients breathed oxygen-enriched air throughout and no other anaesthetic or analgesic drugs were given. Intravenous fluid replacement consisted of Hartmann's solution or blood as indicated clinically. The infusion was generally terminated 10 minutes before the anticipated end of the procedure.

Overall assessments of quality of sedation and ease of control were made and the presence of any side effects noted, particularly in relation to respiratory or airway problems and excitatory phenomena. Immediate recovery was assessed by the times taken from the end of infusion for the patients to open their eyes to command and to give their correct date of birth.

Subsequent psychometric testing was performed at 0.5, 1, 1.5, 2, 3 and 4 hours after the end of the infusion, by an independent investigator who was unaware of the sedative agent used. The patients were questioned at 4 hours about recall of the peri-operative period from arrival in the anaesthetic room until 20 minutes after the return of consciousness. Any side effects and the future acceptability to the patient of the same anaesthetic technique were noted.

Results

There were no significant differences between the groups with respect to patient age, weight or sex (Table 2). The

Table 2. Patient data. Value expressed as mean (SEM)

	Propofol (n = 10)	Midazolam (n = 10)
Age, years	55.1 (7.11)	46.8 (7.22)
Weight, kg	72.0 (4.29)	69.7 (3.29)
Sex, M/F	4/6	5/5

No significant difference between groups.

mean duration of the procedure was similar in the propofol and midazolam groups, 71 and 77 minutes, respectively (Table 3). The mean duration of infusion was 95 minutes for both groups. There were no differences between the groups in the intervals from the start of the infusions to the insertion of the spinal and to skin incision, approximately 7 and 30 minutes, respectively. The mean time to reach the required level of sedation was approximately 26 minutes in both groups.

Quality and ease of control of sedation were good for both groups. Airway maintenance was excellent in all patients; no coughing, laryngospasm, respiratory obstruction or apnoea were observed. No side effects were seen apart from one patient in each group who had restlessness of the arms which required no action. The overall mean

Table 3. Infusion data. Values expressed as mean (SEM) or number of patients, as appropriate.

	Propofol (n = 10)	Midazolam (n = 10)
Duration of procedure, minutes	70.6 (11.97)	76.8 (12.04)
Duration of infusion, minutes	95.4 (12.66)	95.0 (12.16)
Start of infusion to spinal, minutes	7.6 (1.41)	7.0 (0.68)
Start of infusion to incision, minutes	32.1 (2.32)	28.1 (1.83)
Start of infusion to level 4 sedation, minutes	26.6 (1.97)	25.5 (3.91)
Infusion rate, mg/kg/hour	3.73 (0.215)	0.27 (0.098)
Quality of sedation		
Good	10	10
Adequate	0	0
Poor	0	0
Ease of control of sedation		
Good	10	9
Adequate	0	1
Poor	0	0

No significant differences between groups.

infusion rate was 3.73 mg/kg/hour for propofol and 0.27 mg/kg/hour for midazolam.

The mean interval from the end of the infusion until patients could open their eyes and give their date of birth was significantly shorter with propofol than with midazolam, approximately 2 and 10 minutes, respectively (Table 4). Two patients after midazolam were unduly drowsy in

Table 4. Recovery data. Values expressed as mean (SEM).

	Propofol (n = 10)	Midazolam (n = 10)
End of infusion to eyes open, minutes	2.1 (0.348)	9.2 (1.511)*
End of infusion to date of birth, minutes	2.2 (0.359)	10.5 (1.579)*
Number of side effects during recovery	0	2
Instances of recall		
Arrival in anaesthetic room	10	10
Insertion of spinal	8	5
Operative procedure	0	0
Picture at 10 minutes	9	0†
Picture at 20 minutes	9	0†

* $p < 0.005$, † $p < 0.001$, significant differences between groups.

the initial postoperative period and were unable to carry out psychometric testing at 30 minutes in one case and at 1 hour in the other.

Differences were found in patient recall between groups. All patients remembered arrival in the anaesthetic room but only half recalled the spinal injection after midazolam, as opposed to eight out of 10 after propofol. No patient reported awareness of the surgical procedure. Postoperative amnesia was significantly greater after midazolam; no patient had recall at 20 minutes, compared to nine patients after propofol.

All patients were happy with their anaesthetic and would willingly have the same technique again.

Discussion

This study shows that both propofol and midazolam by infusion produce excellent and easily controllable sedation as an adjunct to spinal anaesthesia. However, recovery was significantly faster after propofol with regard both to immediate return of consciousness and orientation and to

subsequent restoration of higher mental function. This is of obvious clinical importance in patients where rapid recovery is desirable, for example for cooperation with postoperative chest physiotherapy. Early postoperative amnesia was significantly greater with midazolam.

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Propofol in total intravenous anaesthesia without nitrous oxide

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Summary

Propofol and methohexitone were evaluated as hypnotics in a total intravenous anaesthesia technique without nitrous oxide in 50 patients of ASA grade 1 or 2. Analgesia was provided by a constant alfentanil infusion and the depth of anaesthesia was controlled by varying the infusion rate of propofol or methohexitone. Induction and intubation responses were smooth and moderate in the propofol group and side effects were few. Control of depth of anaesthesia, blood pressure and pulse rate was relatively easy in this group but more difficult and sometimes inadequate in the methohexitone group, in which side effects were more frequent. The mean infusion rate for propofol was 0.12 mg/kg/minute, similar to those found in studies using nitrous oxide without an opioid. Recovery times were short in both groups but those in the propofol group tended to be shorter. Postoperatively 96% of the propofol patients were clear-headed within 20 minutes, in contrast to only 48% in the methohexitone group.

We conclude that propofol together with alfentanil, both given by a bolus plus infusion technique, provide controllable and satisfactory total intravenous anaesthesia without recourse to nitrous oxide or other inhalational agents. Methohexitone was not as satisfactory as propofol.

Key words

Anaesthetics, intravenous; propofol, methohexitone.

The trend away from inhalational agents and the awareness that nitrous oxide may not be as harmless as was once thought,¹ have prompted the search for new techniques of total intravenous anaesthesia. There are at present few short-acting hypnotics with a wide therapeutic ratio and limited accumulation that are suitable for continuous infusion. Three drugs remain since the withdrawal of Althesin and propanidid: etomidate is currently suspect in continuous infusion, methohexitone has an established place and the new drug propofol requires further assessment.

We therefore set up a randomised, open between-subject study to evaluate the suitability of the emulsion formulation of propofol as a basic hypnotic agent both for induction and maintenance of anaesthesia in an infusion technique in combination with the short-acting opioid alfentanil. The results were compared with a technique that used methohexitone as the hypnotic with alfentanil. The study was approved by the hospital ethical committee and all patients gave informed consent.

Methods

Two groups of 25 patients of ASA grade 1 or 2 and over the age of 18 years, scheduled for medium duration orthopaedic procedures were studied. All received midazolam 7.5 mg orally 1 hour before surgery.

Group 1 received propofol 2–2.5 mg/kg for induction and atracurium 0.5 mg/kg, followed by tracheal intubation and controlled ventilation of the lungs with 33% air in oxygen. The hypnotic was given over 20 seconds; the elderly ASA grade 2 patients received less than the young ASA grade 1 patients. Extra increments of 20 mg were given when necessary. Alfentanil 1 mg (± 15 –20 μ g/kg) was given as a bolus

References

1. MACKENZIE N, GRANT IS. Propofol for intravenous sedation. *Anaesthesia* 1987; **42**: 3–6.
2. HINDMARCH I. Psychomotor function and psychoactive drugs. *British Journal of Clinical Pharmacology* 1980; **10**: 189–209.

after intubation and an alfentanil infusion started at a constant rate of 1 μ g/kg/minute. A propofol infusion was then started at a rate of about 9 mg/kg/hour and the depth of anaesthesia as judged by the clinical signs of blood pressure, pulse rate, pulse width and movement, controlled by varying the rate of this infusion. Extra increments of propofol 10–20 mg were given during maintenance when sudden increases in blood pressure and pulse rate made immediate deepening of anaesthesia necessary. Repeat doses of atracurium were also given when movement occurred. The alfentanil infusion was stopped about 15 minutes before the end of the procedure; the propofol infusion was stopped at the time of skin closure when the relaxant was reversed.

Group 2 received methohexitone 1.5–2 mg/kg instead of propofol for induction and an infusion of about 7 mg/kg/hour for maintenance, with additional increments of 10–20 mg when necessary. Then the protocol as for group 1 was followed.

Pulse rate and blood pressure were recorded at 2-minute intervals throughout the procedure with an automatic non-invasive monitor (Accutor). Induction times and characteristics, effects of intubation and incision, side effects, recovery times and characteristics and postoperative observations were noted, as were the times of administration and dosages of all drugs given.

Finally, the anaesthetist and the surgeon independently graded the anaesthetic procedure as either satisfactory or unsatisfactory; the anaesthetist used criteria of smoothness of induction, control ability of depth of anaesthesia, involuntary movement, unwanted side effects and awakening characteristics, and the surgeon assessed operating conditions and awakening characteristics.

Data are reported as mean values (SEM). Data from the

two groups were compared using the Statistical Analysis System (SAS) package. Student's *t*-test was used for the ordinal data and Fisher's exact test for the nominal data; *p* < 0.05 was considered to indicate significance.

Results

The two groups were comparable as regards ASA grade, weight, age, sex, pre-operative blood pressure and pulse rate, duration of infusions and duration of operation (Table 1).

Table 1. Demographic data. Values expressed as mean (SEM) or number of patients, as appropriate.

	Propofol (<i>n</i> = 25)	Methohexitone (<i>n</i> = 25)
Age, years	32.3 (2.4)	35.7 (2.0)
ASA grade 1/grade 2	22/3	21/4
Weight, kg	59.4 (2.8)	66.6 (2.7)
Sex, M/F	16/9	16/9
Pre-operative mean arterial blood pressure, mmHg	99.3 (2.7)	100.5 (3.8)
Pre-operative heart rate, beats/minute	72 (3.2)	77 (3.4)
Duration of infusion, minutes	64.2 (5.1)	73.6 (6.2)
Duration of operation, minutes	76.6 (5.3)	87.0 (6.3)

The onset of anaesthesia was rapid in both groups (all patients were asleep within 120 seconds), with total induction doses of 2.4 mg/kg for the propofol and 1.7 mg/kg for the methohexitone group. Dosages of all drugs used during induction and maintenance are shown in Table 2. The mean

Table 2. Mean (SEM) drug dosages.

	Propofol (<i>n</i> = 25)	Methohexitone (<i>n</i> = 25)
Induction dose, mg	147.0 (7.0)	113.2 (5.0)
mg/kg	2.4 (0.04)	1.7 (0.03)
Total maintenance dose, mg	453.0 (48.9)	446.8 (43.0)
Maintenance dose, mg/kg/minute	0.12 (0.01)	0.1 (0.00)
Range, mg/kg/minute	0.03–0.19	0.05–0.14

induction dose was 2.4 mg/kg for propofol and 1.7 mg/kg for methohexitone; the maintenance dosages were 0.12 mg/kg/minute or 7.2 mg/kg/hour with propofol and 0.10 mg/kg/minute or 6 mg/kg/hour with methohexitone.

Pain on injection was experienced by one patient in the propofol group and by none in the methohexitone group.

Table 3. Side effects: number of patients.

	Propofol (<i>n</i> = 25)	Methohexitone (<i>n</i> = 25)
Movement during induction	1	15
Movement during maintenance	0	3
Twitch	0	2
Masseter spasm	1	2
Tremor	0	1
Hiccough	0	3
Skin rash	0	1
Hypertension	1	12
Tachycardia	1	12
Practolol given for control of tachycardia	0	7
Naloxone necessary	2	2
Postoperative nausea	0	2
Postoperative restlessness	1	3
Prolonged awakening	1	1

Side effects were commoner in the methohexitone group (Table 3): the most important were involuntary movement, hiccough and unacceptable hypertension and tachycardia. Beta-adrenoceptor blockers were necessary in seven patients to control the heart rate.

Changes in mean blood pressure and pulse rate after induction and intubation and during maintenance are shown in Figs 1 and 2. A 10% decrease in both systolic and diastolic pressures was observed after induction in the propofol group; both increased to 10% above baseline after intubation. The pulse rate increased slightly after induction and further after intubation. Both blood pressure and pulse rate returned to baseline within 10 minutes and remained stable during the rest of the procedure and during the recovery period.

There was a small increase in both diastolic and mean blood pressures after induction in the methohexitone group. Tracheal intubation produced a significantly greater increase in both systolic and diastolic pressures, the latter to well above 100 mmHg, with a significantly greater increase in pulse rate as well. The systolic pressure returned slowly to baseline whilst the diastolic and mean pressures and the pulse rate remained elevated during the rest of the procedure and into the recovery period.

Recovery data are shown in Tables 4 and 5. These include times from the end of operation until spontaneous ventilation and extubation, until patients opened their eyes on command, were orientated (able to give name and birthdate) and could sit up unaided. Patients breathed spontaneously virtually immediately after the end of the operation in both

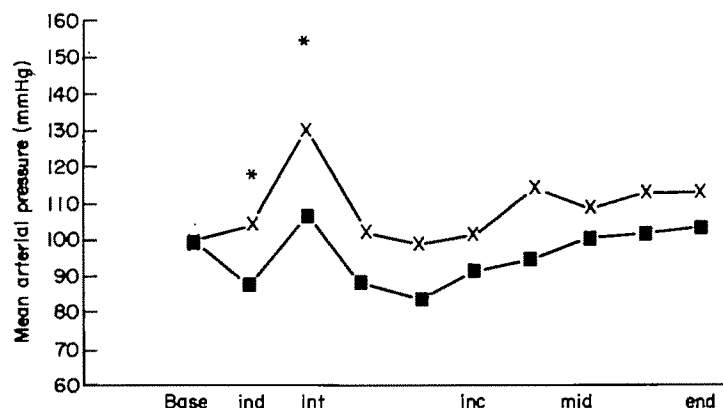


Fig. 1. Mean arterial blood pressure (mmHg) during propofol (■) versus methohexitone (×) study. The marked points indicate mean values (*n* = 25 for each group). Base, pre-operative mean arterial blood pressure; ind, 1 minute after induction; int, 1 minute after intubation; inc, 1 minute after incision; mid, middle of operation; end, end of operation. * *p* < 0.05, Statistically significant differences between the two groups.

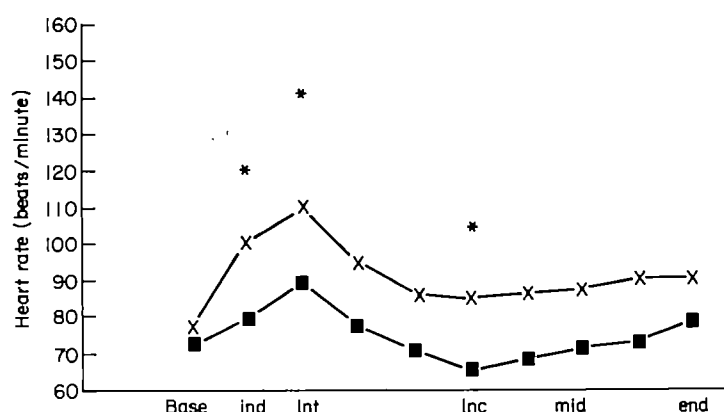


Fig. 2. Heart rates (beats/minute) during propofol (■) versus methohexitone (×) study. The marked points indicate mean values ($n = 25$ for each group). Base, pre-operative heart rate; ind, 1 minute after induction; int, 1 minute after intubation; inc, 1 minute after incision; mid, middle of operation; end, end of operation. * $p < 0.05$, Statistically significant differences between the two groups.

Table 4. Mean (SE) recovery times from end of maintenance infusion.

Time in minutes until:	Propofol ($n = 25$)	Methohexitone ($n = 25$)
End of operation	8.0 (0.8)	7.6 (1.5)
Spontaneous ventilation	9.0 (1.1)	7.5 (1.5)
Extubation	10.3 (1.0)	9.5 (1.9)
Eyes open	12.2 (1.8)	13.2 (1.9)
Orientation	18.9 (2.1)	24.6 (3.1)
Sitting	23.9 (2.1)	28.8 (3.1)

Table 5. Postoperative data.

	Clear-headed within 20 minutes	Pain within 1 hour	Time of administration of analgesic (minutes)
Propofol ($n = 25$)	96% *	76%	44
Methohexitone ($n = 25$)	46%	72%	40

* $p < 0.05$.

groups, 8 minutes after the end of the hypnotic infusions. Most patients' tracheas could be extubated safely 2 minutes later. The other recovery stages were also short in both groups but tended to be shorter in the propofol group, although the differences did not reach statistical significance. Most patients awoke quickly but it was remarkable that all but one in the propofol group (96%) were clear-headed within 20 minutes, in contrast to only 48% in the methohexitone group. The others were sleepy and tended to drift off to sleep again. Postoperative restlessness and nausea were seen more frequently in the methohexitone group. Pain was experienced within one hour in 75% of the patients and by all patients within 2 hours. The average time to the administration of postoperative pain relief was 42 minutes and there were no intergroup differences.

The anaesthetic procedure was rated as satisfactory in 96% of the propofol patients. The surgeon's evaluation of methohexitone anaesthesia was not as poor as the anaesthetist's but it was agreed that the quality was satisfactory in only 56% because of the high incidence of side effects, particularly hiccup, involuntary movements, excessive tachycardia and hypertension during induction, and the difficult management of blood pressure and pulse rate during maintenance.

Discussion

The application of the present anaesthetic infusion technique is simple. All that is needed is two infusion pumps and a ventilator able to supply oxygen-enriched room air. The technique needs practice and meticulous observation of the clinical signs of depth of anaesthesia, because the infusion rates of propofol and methohexitone need frequent adjustment, often in anticipation of changes in surgical stimulus. Arousal may occur suddenly with these very short-acting drugs but no patient awoke during this investigation nor reported awareness when questioned postoperatively. Extra increments of either hypnotic were given when indicated by a sudden increase in blood pressure or pulse rate. The most valuable signs for the assessment of the depth of anaesthesia were changes in systolic and diastolic blood pressure, pulse rate, peripheral pulse width and movement, which required not only deepening of anaesthesia but also a repeat bolus of atracurium. Computerised EEG analysis was not used in this study but adds greatly to control.²

De Grood *et al.*³ reported that the infusion rate had to be decreased from 12 to 6 mg/kg/hour during the course of the anaesthetic for an average patient, whereas we found that the infusion rate remained fairly constant until the end of the procedure. The reason for this may be that de Grood's study was based on gynaecological procedures in which painful stimuli are less than in orthopaedic surgery. The mean maintenance dose of 0.12 mg/kg/minute (7.2 mg/kg/hour) propofol in the present study is within the recommended range for an infusion technique with nitrous oxide but without alfentanil, namely, between 0.1 and 0.2 mg/kg/minute. The infusion rate for methohexitone of 0.1 mg/kg/minute corresponds to that advised by other authors.⁷

The recommended fixed infusion rate for alfentanil of 1 μ g/kg/minute^{7,8} given after a bolus of 1 mg, proved to be a suitable compromise for this technique provided that the infusion was stopped 15 minutes before the end of the operation. A higher or varying rate may improve the stability of anaesthesia but needs earlier discontinuation or it may lead to postoperative respiratory depression. Four patients in this study needed naloxone, two when the alfentanil infusion was stopped too late, and two without any obvious reason.

Communication with the surgeon has to be good, since the timing of the discontinuation of the infusions is critical. This should be about 15 minutes before the end of the procedure for alfentanil and about 8 minutes (at the start of skin closure) for the hypnotic infusion. The duration of the

latter infusion had no influence on the awakening time. Patients awoke within 13 minutes of the end of the infusion even after infusions of 2 hours or more. Two patients, one in each group, showed delayed recovery and were orientated only after one hour.

The frequency and severity of unwanted side effects in the methohexitone group shown in Table 3 are its chief disadvantage and make this drug less suitable. The combination of propofol and alfentanil provides smooth and easily controllable anaesthesia but could have been improved upon had the alfentanil bolus been given before intubation and not afterwards as was called for in the protocol. Nevertheless, the different induction pictures seen with the two drugs suggest that propofol provides better control of autonomic reflexes or a degree of analgesia not offered by methohexitone.

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References

1. SIMMONS K. Some sobering facts about laughing gas. *Journal of the American Medical Association* 1985; **253**: 2334-7.
2. ARCHIBALD JE, DRAZKOWSKI JF. Clinical applications of compressed spectral analysis (CSA) in OR/ICU settings. *American Journal of EEG Technology* 1985; **25**: 13-36.
3. DE GROOT PMRM, RUYS AHC, VAN EGMOND J, BOON LHDJ, CRUL JF. Propofol ('Diprivan') emulsion for total intravenous anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 65-9.
4. DOZE VA, WESTPHAL LM, WHITE PF. Comparison of propofol with methohexitone for outpatient anesthesia. *Anesthesia and Analgesia* 1986; **65**: 1189-95.
5. ROBINSON FP. Propofol ('Diprivan') by intermittent bolus with nitrous oxide in oxygen for body surface operations. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 116-9.
6. ROLLY G, VERSICHELEN L, HERREGODS L. Cumulative experience with propofol ('Diprivan') as an agent for the induction and maintenance of anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 96-100.
7. KAY B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41**: 589-95.
8. STEEGERS PA, BOON LHDJ, PELGROM R. Continuous infusion of alfentanil. *Acta Anaesthesiologica Belgica* 1982; **33**: 81-7.

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Intravenous infusion of propofol for induction and maintenance of anaesthesia during endoscopic carbon dioxide laser ENT procedures with high frequency jet ventilation

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Summary

Fourteen patients of ASA grades 1-3 were anaesthetised with continuous infusions of propofol and alfentanil for endoscopic carbon dioxide laser ENT microsurgery. Their lungs were ventilated with an oxygen-air mixture using a high frequency jet ventilator. Propofol was given at an initial rate of 120 µg/kg/minute for 10 minutes after a bolus dose of 2.6 mg/kg, and then at 80 µg/kg/minute. Alfentanil was given at a rate of 0.5 µg/kg/minute. Arterial pressure decreased significantly after the bolus dose. It increased significantly for a few minutes after laryngoscopy and returned to baseline values during maintenance of anaesthesia. Heart rate increased significantly during induction and until laryngoscopy was performed but it decreased below its initial value after 5 minutes of maintenance. Platelet count and the degree of aggregation did not change during infusion of propofol.

Key words

Anaesthetics, intravenous; propofol.
Ventilation; high frequency jet.

The aim of this study was to evaluate the new formulation of propofol for induction and maintenance of anaesthesia, supplemented with an alfentanil infusion, during endoscopic carbon dioxide laser ENT procedures using high frequency jet ventilation (HFJV). The objective was to assess the effect of a continuous intravenous infusion of propofol on the quality of anaesthesia, haemodynamic status, platelet count and aggregation. Controversy exists in the literature about platelet aggregation: some authors report a decrease in the degree of platelet aggregation with the new vehicle of propofol, while this is not confirmed by others.¹⁻⁵

Methods

Laryngeal surgery was scheduled in 14 patients. Surgical procedures were vocal cord nodule or polyp resection using a carbon dioxide laser. The study was approved by the hospital ethical committee. Patients were premedicated with atropine 0.5 mg and diazepam 10 mg intramuscularly 45 minutes before anaesthesia.

Their lungs were pre-oxygenated on arrival in the operating room. Continuous ECG monitoring (lead D2) was initiated, an indwelling cannula was inserted in an ante-

cubital vein connected to 500 ml dextrose 5% and an arterial catheter was inserted in the radial artery under local anaesthesia. Induction of anaesthesia was carried out with 1 mg of vecuronium followed by slow injection of propofol. Suxamethonium 100 mg was injected after disappearance of the eyelash reflex and the calibrated syringe pumps started.

The initial rate of infusion of propofol, 120 $\mu\text{g/kg/minute}$, was reduced to 80 $\mu\text{g/kg/minute}$ after 10 minutes and supplementary doses were given if necessary; the alfentanil infusion rate was 0.5 $\mu\text{g/kg/minute}$.⁶ Topical anaesthesia of the larynx was achieved with lignocaine 4% to a maximum of 160 mg. The metal jet catheter was fixed inside the Portmann's laryngoscope. The patients' lungs were ventilated with an oxygen-air mixture using a high frequency jet ventilator (Acutronic AMS 1000, Switzerland) and respiratory parameters were adjusted to maintain blood gases in the normal range. A pulse oximeter (Nellcor, California) was attached to the index finger on the opposite side to the arterial catheter. Muscle relaxation was obtained with intermittent bolus doses of vecuronium 1 or 2 mg. Infusions were stopped at the end of the surgery and, if necessary, atropine and neostigmine injected to reverse any residual neuromuscular block.

Arterial blood samples were drawn before induction, for platelet count, platelet factor four (PF4) and thromboglobulin (βTG) plasma dosage. PF4 and βTG were chosen as indicators of platelet aggregation (normal values of PF4 are <15 IU/ml, βTG <56 IU/ml and $\beta\text{TG/PF4}$ 3.8). Induction time was subdivided into two parts: firstly, from the start of propofol injection until the patient stopped counting and secondly, until disappearance of the eyelash reflex. Duration of surgery was also noted. Recovery times were recorded as the time until awakening and resumption of spontaneous breathing, and the time until recall of date of birth.

Arterial blood pressure and heart rate were recorded twice before and once after the induction dose, after the start of laryngoscopy, at different times during the surgical procedure (5, 15, 30, 60 and 69 minutes) and during recovery. Arterial blood samples were drawn in the recovery room, for assessment of platelet count and aggregation. All side effects were recorded from induction to 2 hours after the end of the procedure.

Statistical analysis was performed with the two-tailed Student's paired *t*-test or the two-tailed Wilcoxon signed ranks test as appropriate. Values of $p < 0.05$ were considered to indicate statistical significance.

Results

The mean age of the 14 patients (8 males) was 48.4 years (SEM 3.42, range 17.5–64.6), the mean weight 67.9 kg (SEM 3.55) and the mean height, 166.7 cm (SEM 2.29). Six patients were ASA grade 1, seven were ASA grade 2 and one, ASA grade 3. Two patients presented a pectoral rash at induction but there were no haemodynamic changes or variations in bronchomotor tone. No pain was noted on injection. Maintenance of anaesthesia was satisfactory with the propofol and alfentanil infusion. Heart rate increased significantly after induction ($p = 0.0271$) and during the first few minutes after laryngoscopy but it decreased below initial values during the surgical procedure (Fig. 1). Systolic ($p = 0.0003$, Fig. 2) and diastolic ($p = 0.0067$, Fig. 3) arterial blood pressures decreased significantly after induction and increased significantly after laryngoscopy (systolic, $p = 0.0358$; diastolic, $p = 0.0013$). No side effects were observed during maintenance.

The mean propofol induction dose was 177.14 mg (2.6 mg/kg, SEM 0.13) and 10 patients received a mean sup-

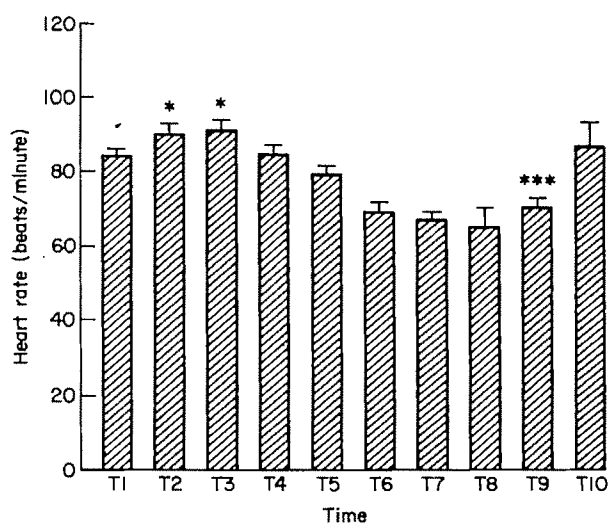


Fig. 1. Mean (SEM) heart rate. * $p < 0.05$, *** $p < 0.001$. T1, Before bolus dose; T2, after bolus dose; T3, after intubation; T4, T5, T6, T7, T8, after 5, 15, 30, 45 and 60 minutes of maintenance; T9, end of propofol infusion; T10, patient awake.

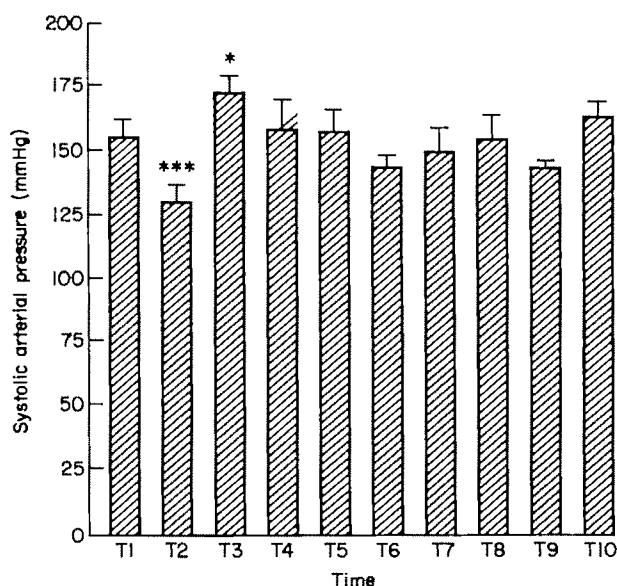


Fig. 2. Mean (SEM) systolic arterial blood pressure. * $p < 0.05$, *** $p < 0.001$. See Fig. 1 for times.

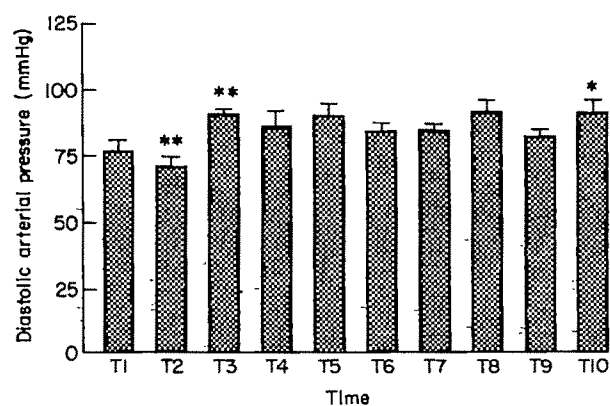


Fig. 3. Mean (SEM) diastolic arterial blood pressure. * $p < 0.05$, ** $p < 0.01$. See Fig. 1 for times.

Table 1. Duration of induction, surgery and recovery. Values expressed as mean (SEM), range

Induction time until cessation of counting, seconds	33.14(3.40), 10–50
Total induction time, seconds	62.86(5.49), 23–90
Surgical time, minutes	54.36(11.70), 13–189
Recovery time until patients awake and breathing spontaneously, minutes	10.93 (0.78), 5–15
Total recovery time until patients fully orientated, minutes	12.79(0.81), 7–18

Table 2. Platelet count and aggregation factors. Values expressed as mean (SEM).

	Pre-operative	Postoperative	
Platelet count	260 500.00(18 148.00)	256 875.00(16 567.00)	p = 0.9922
PF4, IU/ml	15.46(3.90)	15.34(3.81)	p = 0.9883
β TG, IU/ml	105.00(16.09)	97.62(19.20)	p = 0.9779
β TG/PF4	8.22(0.72)	7.67(0.69)	p = 0.9766

plementary dose of 76.5 mg (SEM 10.6) during maintenance. The mean alfentanil dose was 1.71 mg (SEM 0.3) and the mean dose of vecuronium, 7 mg (SEM 1.2). Durations of induction, surgery and recovery are in Table 1.

There was no statistically significant difference between the pre- and postoperative values for platelet count and factors of aggregation (PF4, β TG, β TG/PF4). (Table 2). No side effects were observed in the recovery room.

Discussion

The carbon dioxide laser for laryngeal surgery is dangerous in the presence of inflammable tracheal tubes.⁷ HFJV is the technique of choice to avoid this problem and to give good surgical access. The diameter of the ventilatory needle used with HFJV is so small that it requires a high pressure of insufflation and total intravenous anaesthesia is necessary since vaporizers are not functional at this pressure. We chose propofol because of its short half-life and good quality of recovery.

Several studies^{8–10} have reported pain on injection but none of our patients mentioned any discomfort. This may be due to the large diameter of the vein we used for injection. The time to cessation of counting was relatively long in comparison with other studies because we injected propofol slowly to minimise haemodynamic effects. Systolic arterial pressure after induction decreased by 16.24% from the baseline value; the decreases were 9.5% and 13%, respectively, for the diastolic and mean pressures. These results are in agreement with the literature.^{11,12} Laryngoscopy increased arterial pressure significantly but arterial pressure returned to the baseline value after a few moments although the procedure was continued. This finding is also similar to that of previous studies.^{13,14}

Alfentanil, a rapidly acting analgesic with a short half-life, was given by continuous infusion to decrease the marked haemodynamic and endocrine variations that occur with laryngoscopy, since propofol has no major analgesic property. The use of alfentanil was not associated with apnoea.

The time to recall of date of birth, 12.8 minutes, was similar to that observed by Kay,⁶ although De Grood *et al.*⁸ noted a somewhat longer recovery time of 22 minutes. The quality of recovery was excellent; in the recovery room the patients were, and stayed, fully alert and orientated.

The new formulation of propofol is based on a fat emulsion (Intralipid[®]). A haematological modification that has been associated with Intralipid[®] is a reduction in the adhesiveness of platelets. There was no change in platelet

count in our study; this is in accordance with the findings of Sear *et al.*¹⁵ Postoperative PF4, β TG levels and β TG/PF4 were slightly lower than pre-operative values in our study of aggregation, although the difference was not statistically significant. Stress with its adrenergic response can stimulate platelets and produce the release of specific proteins (PF4 and β TG) from their α granules. This may explain the somewhat higher pre-induction levels of PF4 and TG. The most important fact is that there was no increase in the values during propofol infusion. No variation in platelet aggregation is observed in animals.¹⁶

In conclusion, propofol and alfentanil infusions with

vecuronium provide good operative conditions for endoscopic carbon dioxide laser ENT surgery. Platelet count and aggregation do not seem to be affected by the new formulation of propofol.

Acknowledgments

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References

- KAPP JP, DUCKERT F, HARTMANN G. Platelet adhesiveness and serum lipids during and after intralipid infusions. *Nutrition and Metabolism* 1971; **13**: 92–9.
- CRONBERG S, NILSSON IM. Coagulation studies after administration of a fat emulsion, Intralipid. *Thrombosis, Diathermy and Haemorrhage* 1967; **18**: 664–9.
- DAY HJ, FEWELL W, SOLOFF LA. Thrombosis in the dog produced by single rapid infusion of long-chain saturated fatty acids. *American Journal of the Medical Sciences* 1967; **253**: 83–93.
- DUBBER AHC, RIFKIND B, GALE M, McNICOL GP, DOUGLAS AS. The effect of fat feeding on fibrinolysis Stypven time and platelet aggregation. *Journal of Atherosclerotic Research* 1967; **7**: 225–35.
- GLUECK HJ, VITERI FE. The effect of intravenously administered fat on the coagulation mechanism. *American Journal of Clinical Nutrition* 1963; **13**: 8–24.
- KAY B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41**: 589–95.
- GUSSACK GS, EVANS RF, TACCHI EJ. Intravenous anesthesia and jet ventilation for laser microlaryngeal surgery. *Annals of Otolaryngology and Laryngology* 1987; **96**: 29–33.
- DE GROOD PMRM, COENEN LGJ, VAN EGMOND J, BOUJ LHDJ, CRUL JF. Propofol emulsion for induction and maintenance of anaesthesia. A combined technique of general and regional anaesthesia. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 219–23.
- HYNNEN M, KORTILA K, TAMMISTO T. Pain on IV injection of propofol (ICI 35868) in emulsion formulation. Short communication. *Acta Anaesthesiologica Scandinavica* 1985; **29**: 651–2.
- FAHY LT, VAN MOURIK GA, UTTING JE. A comparison of the induction characteristics of thiopentone and propofol (2,6-diisopropylphenol). *Anaesthesia* 1985; **40**: 939–44.
- HERREGODS L, ROLLY G, VERSICHELEN L, ROSSEEL MT. Propofol combined with nitrous oxide-oxygen for induction and maintenance of anaesthesia. *Anaesthesia* 1987; **42**: 360–5.

12. EDELST G. A comparison of propofol and thiopentone as induction agents in outpatient surgery. *Canadian Anaesthetists' Society Journal* 1987; **34**: 110–6.
13. MILLAR FORBES A, DALLY FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42**: 618–24.
14. WARK KJ, LYONS J, FENECK RO. The hemodynamic effects of bronchoscopy. Effect of pretreatment with fentanyl and alfentanil. *Anaesthesia* 1986; **41**: 162–7.
15. SEAR JW, UPPINGTON J, KAY NH. Haematological and biochemical changes during anaesthesia with propofol. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 165–8.
16. GLEN JB, HUNTER SC, BLACKBURN TP, WOOD P. Interaction studies and other investigations of the pharmacology of propofol. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 7–14.

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Anaesthesia for extracorporeal shock-wave lithotripsy. A comparison of propofol and methohexitone infusions during high frequency jet ventilation

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Summary

A continuous infusion of propofol 2.0–2.5 mg/kg for induction followed by 9 mg/kg/hour for the first 30 minutes and 6 mg/kg/hour thereafter, was compared with methohexitone 1.5 mg/kg for induction followed by 4.8 mg/kg/hour thereafter for maintenance of anaesthesia in a randomised study of 40 patients who underwent extracorporeal shock-wave lithotripsy using high frequency jet ventilation (HFJV). Systolic blood pressure was significantly lower in the propofol group after induction of anaesthesia, tracheal intubation, placement in the semirecumbent position in the hoist, bath immersion and after 5, 10 and 30 minutes of treatment. Diastolic blood pressure was significantly lower in the propofol group after intubation, placement in the hoist, bath immersion and after 5, 10 and 15 minutes of treatment. Heart rate was significantly lower in the propofol group after induction, intubation, placement in the hoist and bath immersion. There was no significant difference in the quality of induction between the two groups. Quality of maintenance of anaesthesia was judged to be poor in six out of 20 patients who received methohexitone compared with one out of 20 who received propofol but this difference did not reach statistical significance. There was no significant difference between the recovery times for the two groups but six out of 20 patients who received methohexitone were judged to have a poor recovery from anaesthesia compared with none in the propofol group ($p < 0.05$). Propofol was associated with excellent induction, maintenance and recovery characteristics but it had a propensity to produce greater decreases in blood pressure, which were most marked when the patient was placed in the semirecumbent position in the hoist.

Key words

Anaesthetics, intravenous; propofol, methohexitone.
Surgery; extracorporeal shock wave lithotripsy.

Extracorporeal shock-wave lithotripsy (ESWL) is a technique for noninvasive renal stone destruction in which the energy produced by multiple underwater electrical discharges is focussed to a point at which the patient's stone is positioned.^{1,2} The procedure is painful and is therefore performed under regional or general anaesthesia.^{3–5} The latter has the advantage that respiratory excursion and other movement can easily be controlled. It has been suggested that high frequency jet ventilation (HFJV) is advantageous for the procedure because stone movement can be virtually abolished. This facilitates stone placement in the target zone and possibly increases the hit rate of the shock waves.^{6,7} The use of inhalational agents can be a problem during HFJV maintenance of general anaesthesia because it is difficult to deliver a known concentration of anaesthetic vapour to the alveoli. This may be overcome by the use of a continuous intravenous technique.

The agents that satisfy the pharmacokinetic criteria for continuous intravenous anaesthesia are few since the withdrawal of Althesin and the problem of adrenocortical suppression associated with etomidate infusions,⁸ and in practice the choice lies between the use of either methohexitone or propofol. Comparison of these two agents indicates that propofol provides better anaesthesia and

recovery characteristics but it is associated with greater cardiovascular depression than methohexitone.^{9,10}

The cardiovascular effects of propofol are of particular relevance to ESWL because it is a procedure that may be associated with major changes in cardiovascular variables.^{5,11} These arise because of the change in posture when the patient is placed in the semirecumbent position in the hoist, and the subsequent immersion in a bath of water maintained at 37°C. Marked hypotension has been documented during positioning in the hoist and although this is invariably reversed on immersion in patients who undergo regional blockade, persistent hypotension may occur in patients who undergo general anaesthesia.⁵ We present here the results of a comparative evaluation of propofol and methohexitone infusions for maintenance of anaesthesia during ESWL using HFJV.

Methods

Forty patients of ASA grades 1–3 and between the ages of 18 and 65 years were studied. Treated or untreated hypertensive patients and those with ischaemic heart disease were not studied. All patients had haemoglobin, urea and electrolyte values within normal limits and none had clinical or

suspected hepatic disease. Patients over 50 years had a normal ECG and chest X ray. Informed patient consent was obtained and the patients were randomly allocated into two groups of twenty. All patients were unpremedicated and received a fluid load of Hartmann's solution 5 ml/kg prior to induction of general anaesthesia.

Anaesthesia in group 1 was induced with fentanyl 1 $\mu\text{g}/\text{kg}$, 1% propofol 2.0–2.5 mg/kg injected over 40 seconds and vecuronium 1 mg/kg. The trachea was intubated 2 minutes after induction, using a Mallinckrodt Hi-Lo jet tube after the vocal cords had been sprayed with 1% lignocaine solution. Anaesthesia was maintained from induction onwards with a continuous infusion of propofol 9 mg/kg/hour for the first 30 minutes and 6 mg/kg/hour thereafter, delivered via an Injectomat S4 syringe pump. Supplements of vecuronium 1–2 mg were administered as necessary to maintain paralysis during the procedure.

The same anaesthetic technique was used in group 2 except that 1% methohexitone 1.5 mg/kg was used for induction, and anaesthesia was maintained with a continuous infusion of methohexitone 4.8 mg/kg/hour for the duration of the procedure.

After tracheal intubation the lungs of all patients were manually ventilated via a Bain system that delivered 50% nitrous oxide in oxygen (fresh gas flow 100 ml/kg), until immersion in the water bath maintained at 37–38°C. Jet ventilation with an AMS 1000 Universal Jet Ventilator (Acutronic) was then initiated via the side channel of the

Mallinckrodt Hi-Lo jet tube. This was set to deliver a humidified gas mixture of 50% nitrous oxide in oxygen at a rate of 150 breaths/minute with 30% inspiratory time. The Bain system was used for gas entrainment to deliver a fresh gas flow of 100 ml/kg 50% nitrous oxide in oxygen with the expiratory valve open to atmospheric pressure. Oxygenation was monitored with a Biox III oximeter and end tidal carbon dioxide measured at 5–10-minute intervals by interruption of the jet ventilation and delivery of a single large breath manually via the Bain system.^{12,13} End tidal carbon dioxide readings were maintained in the range 4.0–5.0 kPa by appropriate adjustment to the jet driving pressure. Arterial blood pressure was measured with a Dinamap automatic blood pressure monitor and intravenous bolus doses of ephedrine 3–12 mg were administered whenever decreases >25% of the pre-induction mean arterial blood pressure were noted. The electrocardiogram was monitored throughout.

Depth of anaesthesia was assessed by monitoring pupil size, cardiovascular variables and the presence of sweating. A supplement of fentanyl 1 $\mu\text{g}/\text{kg}$ was given if anaesthesia was judged to be inadequate and the infusion rate increased by 10–20% until a satisfactory state was achieved. The infusion was discontinued at the end of the procedure when the last shock wave had been delivered and residual paralysis reversed with neostigmine 2.5 mg and glycopyrronium 0.6 mg.

Systolic, diastolic and mean arterial blood pressures and

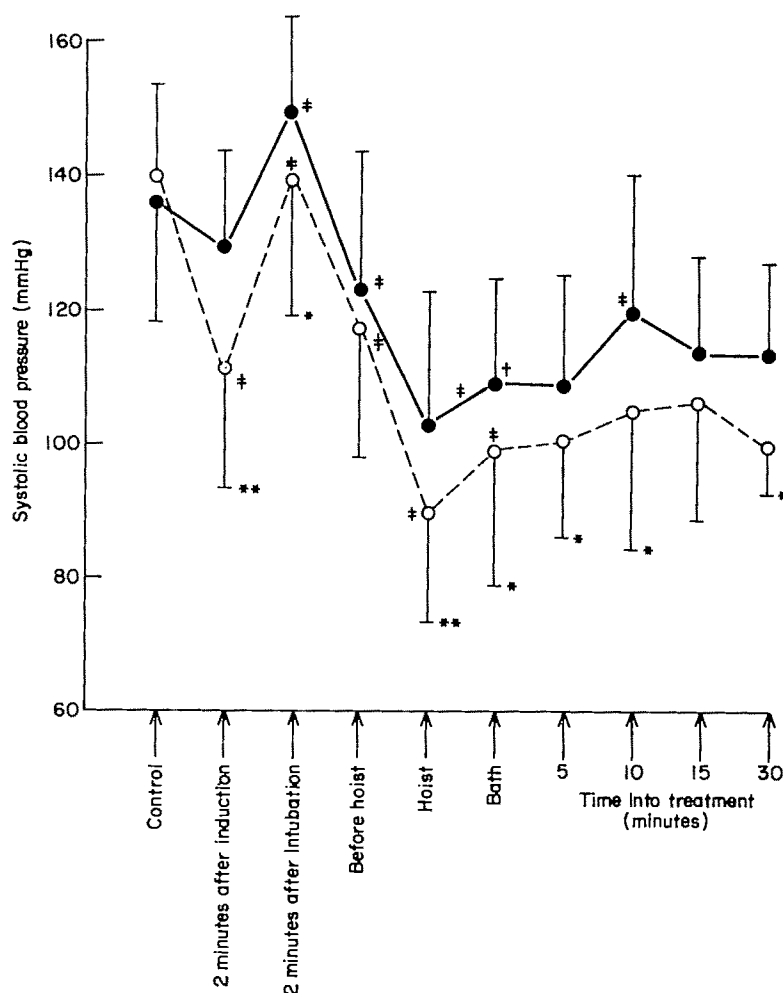


Fig. 1. Mean (SD) systolic arterial pressure at indicated stages of the procedure. —, Methohexitone; ---, propofol. * $p < 0.05$, ** $p < 0.01$, significant differences between groups (unpaired t -test); † $p < 0.05$, ‡ $p < 0.01$, significant differences compared with preceding stage (paired t -test)

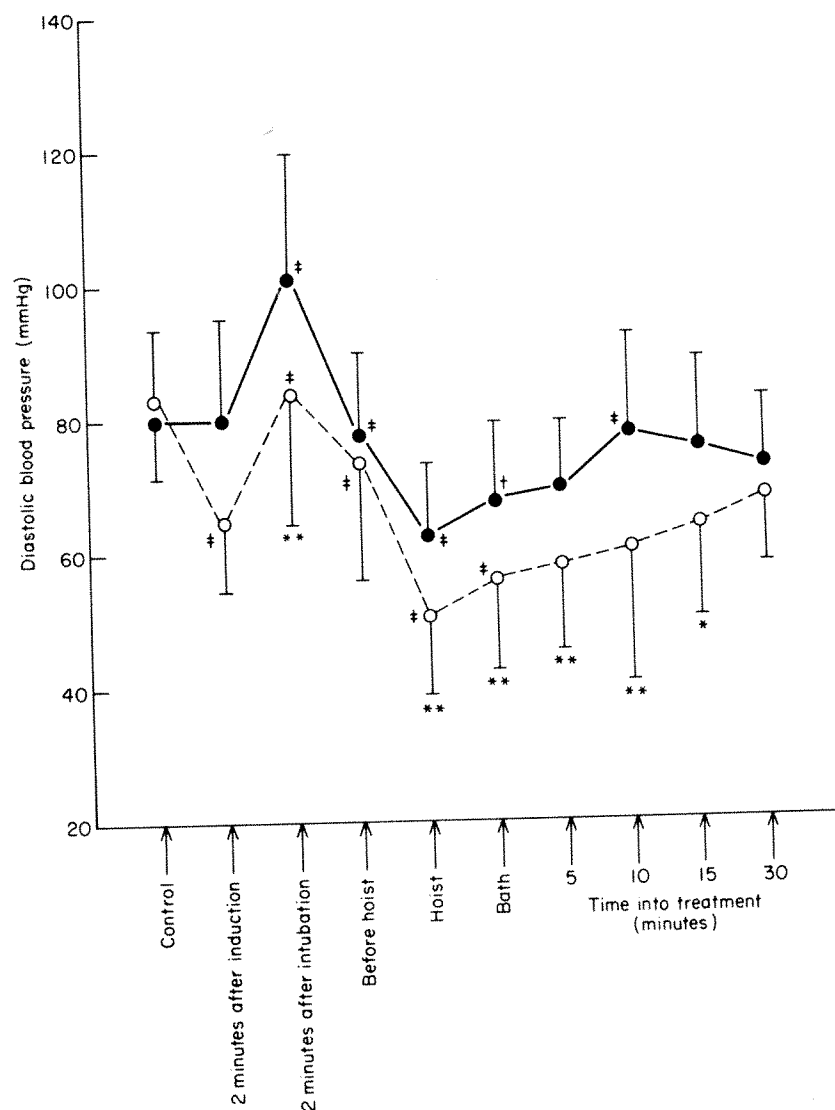


Fig. 2. Mean (SD) diastolic arterial pressure at indicated stages of the procedure. —, Methohexitone; ----, propofol * $p < 0.05$, ** $p < 0.01$, significant differences between groups (unpaired t -test); † $p < 0.05$, ‡ $p < 0.01$, significant differences compared with preceding stage (paired t -test).

heart rate were recorded before induction, 2 minutes after induction, 2 minutes after intubation, before and after placement in the hoist in the semirecumbent position, after immersion in the bath and at 5-minute intervals during treatment. The requirement for intravenous ephedrine was noted, together with the occurrence of hiccough, pain or movement on induction, the requirement for supplementary fentanyl or increased rate of infusion as judged by pupil size, cardiovascular status and the presence of sweating, and the times from the end of the infusion until return of response to verbal command to open eyes and the ability to give correct date of birth and day of week. We also recorded the time at which patients were considered fit for discharge from the recovery room, immediate postoperative requirements for opioid analgesics and antiemetics and the incidence of awareness on direct questioning. A subjective assessment (good or poor) was made by the operators of the overall quality of induction, maintenance and recovery from anaesthesia.

The significance of the results for between-group comparisons was assessed for binary outcome variables by the Chi-squared test with Yates' correction and for continuous outcome variables by unpaired t -tests. Paired t -tests were used for changes within each group.

Table 1. Patient demography and duration of infusions. Values expressed as mean (SD).

	Age, years	Weight, kg	Sex, M/F	Duration of infusions, minutes
Methohexitone (n = 20)	40.1 (11.1)	71.7 (17.7)	13/7	40.3 (15.9)
Propofol (n = 20)	45.7 (11.3)	69.5 (11.1)	14/6	39.3 (14.1)

Results

The two groups were comparable for age, weight and duration of anaesthesia (Table 1). The changes in arterial blood pressure associated with the various stages of the procedure are shown in Figs 1 and 2. There were no significant differences between the groups in respect of the pre-induction systolic and diastolic blood pressures and heart rate. The general trend in both groups was for blood pressure to decrease on induction of anaesthesia, to increase after intubation, decrease on placement in the hoist and then to increase slightly again after immersion in the bath and onset of treatment.

Patients in the propofol group experienced a greater decrease in systolic arterial pressure during induction ($p <$

0.01) while patients in the methohexitone group exhibited greater increases in systolic ($p < 0.05$) and diastolic pressure ($p < 0.01$) at intubation. Systolic and diastolic pressures decreased more markedly in the propofol group compared with methohexitone ($p < 0.01$) on placement in the semi-recumbent position.

Fifteen out of 20 patients in the propofol group received intravenous boluses of ephedrine to counteract decreases in mean arterial pressure $>25\%$ of the pre-induction level when they were positioned in the hoist. This compared with four out of 20 in the methohexitone group ($p < 0.05$). The systolic and diastolic arterial pressures continued to be consistently lower in the propofol group than in the methohexitone group during treatment itself. This difference reached statistical significance at 5, 10 and 30 minutes ($p < 0.05$) for the systolic pressures and at 5, 10 ($p < 0.01$) and 15 minutes ($p < 0.05$) for the diastolic pressures.

The changes in heart rate are shown in Fig. 3. Propofol was associated with a consistently lower heart rate throughout the procedure. This difference was statistically significant after induction ($p < 0.01$), intubation ($p < 0.01$), before and after placement in the hoist ($p < 0.05$) and after immersion in the bath ($p < 0.05$).

There was no difference between the groups in respect of the incidence of pain, hiccuph or movement during induction, and the quality of induction was judged to be equally good in both groups (Tables 2 and 3). The general

Table 2. Number of patients in each group who had pain, hiccuph or excessive movement on induction.

	Pain	Hiccuph	Movement
Methohexitone ($n = 20$)	2	5	2
Propofol ($n = 20$)	2	2	1

quality of maintenance of anaesthesia as judged by the need for supplementary fentanyl or increase in infusion rate, was considered to be poor in six patients in the methohexitone group compared with one in the propofol group (Table 3). One patient who received methohexitone reported a brief period of awareness which did not cause any undue distress.

There was no difference between the groups in the immediate postoperative requirements for opioid analgesics or antiemetics (Table 4). Similarly, there were no significant differences between the methohexitone and propofol groups

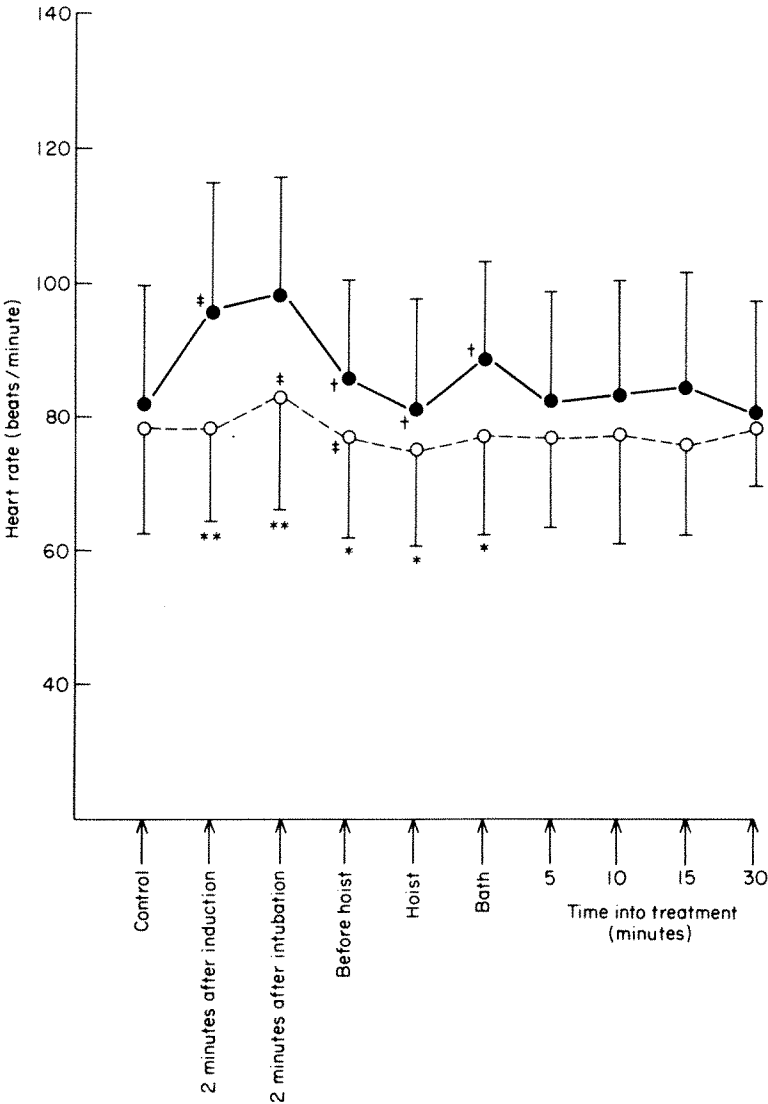


Fig. 3. Mean (SD) heart rate at indicated stages of the procedure. —, Methohexitone; ---, propofol. * $p < 0.05$, ** $p < 0.01$, significant differences between groups (unpaired t -test); † $p < 0.05$, ‡ $p < 0.01$, significant differences compared with preceding stage (paired t -test)

Table 3. Subjective assessment (good/poor) of the quality of induction, maintenance and recovery from anaesthesia in the two groups ($n = 20$ each group).

	Induction		Maintenance		Recovery	
	Methohexitone	Propofol	Methohexitone	Propofol	Methohexitone	Propofol
Good	17	19	14	19	14	20
Poor	3	1	6	1	6	0*

* $p < 0.05$.

Table 4. Number of patients in each group who required immediate postoperative opioid analgesia or antiemetics.

	Analgesia	Antiemetics
Methohexitone ($n = 20$)	4	3
Propofol ($n = 20$)	2	1

Table 5. Mean (SD) times from end of infusion until return of ability to open eyes to command, to give correct date of birth and day of week and until fitness for discharge from the recovery room.

Time in minutes until:	Methohexitone ($n = 20$)	Propofol ($n = 20$)
Eyes open	7.4 (2.2)	7.8 (3.3)
Date of birth	12.7 (8.9)	10.0 (4.1)
Day of week	14.3 (6.7)	10.5 (5.4)
Fit for discharge from recovery room	86.8 (68.0)	60.2 (35.1)

for the times taken for return of response to verbal command to open eyes, ability to give correct date of birth and day of week, and fitness for discharge from the recovery room (Table 5). However, the overall quality of recovery was judged to be poor in six patients in the methohexitone group compared with none in the propofol group ($p < 0.05$, Table 3).

Discussion

Anaesthesia for ESWL may be achieved using general anaesthesia and conventional intermittent positive pressure ventilation but HFJV offers the advantage of decreased stone movement because of minimal respiratory excursion and a consequent higher hit rate of shock waves in the target zone.^{6,7} The system described in this study permits the use of a controlled mixture of nitrous oxide and oxygen for both the jet ventilator and entrainment but adequate anaesthesia cannot be guaranteed and it was therefore considered necessary to supplement the technique with a continuous infusion of an intravenous agent. Previous studies have indicated that propofol and methohexitone are suitable for use in this manner.^{9,10} Propofol, in particular, has the advantage of ease of control of the level of narcosis and a faster recovery time but it has a greater depressive effect on the cardiovascular system. This may be of particular relevance to ESWL because the technique involves placement of the patient in the semirecumbent position followed by water immersion, and considerable haemodynamic changes may occur.^{5,11}

The results of this study show clearly that the use of propofol as an infusion is associated with a greater degree of hypotension than methohexitone. The decrease in blood pressure on positioning in the hoist was very marked in some patients and most (15/20) required the administration of ephedrine at this stage. In contrast, only four of the 20 patients in the methohexitone group required ephedrine. The heart rate was also significantly lower in the propofol group from the period of induction to immersion in the bath and showed little change from positioning in the hoist

onwards, despite the fact that 15 of the 20 patients had received ephedrine during this period.

Our observations with regard to the ease of maintenance of anaesthesia with the two regimens are in accord with the findings of Kay.⁹ Six of the 20 patients who received methohexitone were judged to have poor maintenance of anaesthesia and one patient reported a brief period of awareness.

The dose of 4.8 mg/kg/hour (80 μ g/kg/minute) for methohexitone in this study approximates the 75.9 μ g/kg/minute calculated by Sear and co-workers¹⁴ to be that required to suppress the initial response to surgical incision in 95% of morphine premedicated patients who receive continuous infusion anaesthesia to supplement 67% nitrous oxide in oxygen. The patients in the present study were unpremedicated but received fentanyl 1 μ g/kg at induction. It is possible that a higher infusion rate may provide better maintenance of anaesthesia but it may also result in accumulation of the drug. It has been suggested that this will occur after administration of a total dose that exceeds 600–800 mg.¹⁵

The times until patients opened their eyes to command and were able to give correct date of birth and day of week were not significantly different between the two groups but these are very crude indices of recovery from anaesthesia. The overall impression of the operators and recovery staff was that recovery was better in the propofol group. This is consistent with the results of other studies which demonstrate superior recovery characteristics of propofol compared with methohexitone.^{9,10}

In conclusion, both methohexitone and propofol used as a continuous infusion for ESWL proved to be acceptable anaesthetic agents and facilitated the use of HFJV, which provides good conditions for the shock-wave treatment. However, propofol has a propensity to cause marked hypotension when the patient is positioned in the hoist. In this respect, the greater haemodynamic stability of methohexitone indicates that it should be the agent of choice for any patient whose cardiovascular status may be less than optimal.

Acknowledgments

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References

1. CHAUSSEY CH, BRENDEN W, SCHMIEDT E. Extracorporeally induced destruction of kidney stones by shock waves. *Lancet* 1980; **2**: 1265–8.
2. PALFREY ELHP, BULTITUDE MI, CHALLAH S, PEMBERTON J, SHUTTLEWORTH KED. Report of the first 1000 patients treated at St Thomas' Hospital by extracorporeal shockwave lithotripsy. *British Journal of Urology* 1986; **58**: 573–7.
3. ABBOTT MA, SAMUEL JR, WEBB DR. Anaesthesia for extracorporeal shock wave lithotripsy. *Anaesthesia* 1985; **40**: 1065–72.
4. FRANK M, MCATEER EJ, COHEN DG, BLAIR IJ. One hundred

- cases of anaesthesia for extracorporeal shock wave lithotripsy. *Annals of the Royal College of Surgeons* 1985; **67**: 341-3.
5. RICKFORD JR, SPEEDY HM, TYTLER JA, LIM M. Comparative evaluation of general, epidural and spinal anaesthesia for extracorporeal shock wave lithotripsy. *Annals of the Royal College of Surgeons* 1987 (in press).
 6. SCHULTE AM, ESCH J, KOCHS E, MEYER WH. Improved efficiency of extracorporeal shock wave lithotripsy during high frequency jet ventilation. *Anesthesiology* 1985; **63**: A177.
 7. CARLSON CA, BOYSEN PG, BANNER MJ, GRAVENSTEIN JS. Conventional vs high frequency jet ventilation for extracorporeal shock wave lithotripsy. *Anesthesiology* 1985; **63**: A350.
 8. OWEN H, SPENCE AA. Etomidate. *British Journal of Anaesthesia* 1984; **56**: 555-7.
 9. KAY B. Propofol and alfentanil infusion. A comparison with methohexitone and alfentanil for major surgery. *Anaesthesia* 1986; **41**: 589-95.
 10. JESSOP E, GROUNDS RM, MORGAN M, LUMLEY J. Comparison of infusions of propofol and methohexitone to provide light general anaesthesia during regional blockade. *British Journal of Anaesthesia* 1985; **57**: 1173-7.
 11. WEBER W, MADLER G, KEIL B, POLLWEIN B, LAUBENTHAL H. Cardiovascular effects of ESWL. In: GRAVENSTEIN JS, PETER K, eds. *Extracorporeal shock-wave lithotripsy for renal stone disease*. London: Butterworths, 1986: 101-12.
 12. MIHM FG, FEELEY TW, RODARTE A, ASHTON JPA. Monitoring high frequency jet ventilation by end-tidal carbon dioxide concentration. *Anesthesiology* 1982; **57**: A87.
 13. CARLSON CA, GRAVENSTEIN JS, BANNER MJ, BOYSEN PG. Monitoring techniques during anaesthesia and HFJV extracorporeal shock-wave lithotripsy. *Anesthesiology* 1985; **63**: A178.
 14. SEAR JW, PHILLIPS KC, ANDREWS CJH, PRYS-ROBERTS C. Dose-response relationships for infusions of Althesin or methohexitone. *Anaesthesia* 1983; **38**: 931-6.
 15. SEAR JW. General kinetic and dynamic principles and their application to continuous infusion anaesthesia. *Anaesthesia* 1983; **38** (Suppl.): 10-25.

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An open comparison of propofol and enflurane for prolonged abdominal operations

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Summary

Anaesthesia in 15 patients scheduled for prolonged abdominal surgery was induced with hexobarbitone and maintained with nitrous oxide and enflurane, while in a further 15 patients propofol was used for induction and maintenance. Three patients in the latter group required additional fentanyl but cardiovascular responses were otherwise similar in the two groups. Return of consciousness, response to verbal command, ability to answer questions and adequate spontaneous ventilation was more rapid in the propofol patients. EEG power spectra also returned to baseline more rapidly in the propofol group.

Key words

*Anaesthetics, intravenous; propofol.
Anaesthetics, volatile; enflurane.*

Propofol has been used mainly for induction of anaesthesia and for short procedures^{1,2} but its pharmacokinetics³ suggest that it could be used for a longer duration without accumulation. The present study investigated the use of propofol for procedures that lasted more than 2 hours and compared its effects with those of a standard method using isoflurane.

Methods

Thirty patients were premedicated with pethidine 0.5 mg/kg, promethazine 1.0 mg/kg and atropine 0.01 mg/kg intramuscularly 45 minutes prior to induction of anaesthesia and randomly allocated to one of two groups. Anaesthesia in 15 patients was induced with hexobarbitone 3 mg/kg and the trachea intubated after suxamethonium 1.0 mg/kg. Maintenance was with nitrous oxide and oxygen 2:1 with enflurane 0.5-2.5%. Anaesthesia in the second group was induced with propofol 2.0 mg/kg and maintained with an infusion of 100 µg/kg/minute plus nitrous oxide in oxygen 2:1. Pancuronium was used to maintain muscle relaxation in both groups and the lungs were ventilated to normocapnia. Fentanyl 0.1 mg was used for additional analgesia as indicated by increases in heart rate and arterial pressure of 25% above control.

A radial artery was cannulated and the ECG displayed

continuously. The EEG power spectra were derived (position Fp1-A3) before, during and after anaesthesia in the frequency wavebands delta (0.5-4.0 Hz), theta (4.0-8.0 Hz), alpha (8.0-13.0 Hz) and beta (13.0-30.0 Hz) using the Lifescan cerebral monitor (Neurometrics, San Diego, USA).

Residual neuromuscular blockade at the end of surgery was reversed with neostigmine. The time to spontaneous respiration was noted, as was the time to orientation in time and space. Arterial blood gases were measured 10 minutes after tracheal extubation.

Table 1. Demographic data. Values expressed as mean (range) or number of patients, as appropriate.

	Group 1 (enflurane) (n = 15)	Group 2 (propofol) (n = 15)
Age, years	57 (36-82)	60 (24-84)
Sex, M/F	7/8	5/10
Weight, kg	79 (52-94)	63 (53-74)
Height, cm	172 (152-191)	165 (154-178)
ASA grade 1	2	4
grade 2	12	10
grade 3	1	1
Duration of anaesthesia, (minutes)	201 (131-336)	168 (123-258)

Table 2. Number of side effects observed during the two anaesthetic techniques and anaesthetists' assessment for prolonged abdominal surgery.

	Group 1 (enflurane) (n = 15)	Group 2 (propofol) (n = 15)
<i>Induction characteristics</i>		
Pain at site of injection	0	3
<i>Maintenance characteristics</i>		
Hypotension	6	5
Bradycardia	0	1
Hiccough	3	1
<i>Early recovery characteristics</i>		
Sedation	4	1
Drowsiness	11	0
Nausea	2	0
Vomiting	1	0
<i>Anaesthetists' assessment</i>		
Good	13	12
Adequate	2	2
Poor	0	1

Table 3. Recovery times from end of maintenance. Values expressed as mean (range).

	Group 1 (enflurane) (n = 15)	Group 2 (propofol) (n = 15)
<i>Time in minutes until:</i>		
Start of spontaneous ventilation	6.5 (4-12)	9.3 (3-55)
Adequate spontaneous ventilation	17.0 (9-24)	13.5 (4-71)
Extubation	19.8 (10-28)	14.7 (4-75)
First reaction to verbal command	16.3 (8-15)	10.3 (3-58)*
Patient coordinated	20.1 (11-32)	14.7 (6-67)*
Orientation to time and space (after extubation)	14.6 (5-17)	2.3 (1-5)*

*p < 0.05.

Table 4. Arterial oxygen and carbon dioxide tensions (P_{iO_2} 0.21) of spontaneously breathing patients. Values expressed as mean (range).

	Group 1 (enflurane) (n = 15)	Group 2 (propofol) (n = 15)
<i>P_aO₂, kPa</i>		
Before induction	10.2 (8.1-11.9)	10.4 (7.9-12.1)
10 minutes after extubation	9.4 (7.2-10.9)	10.1 (8.0-11.0)
<i>P_aCO₂, kPa</i>		
Before induction	5.2 (4.7-5.8)	5.1 (4.5-5.7)
10 minutes after extubation	5.4 (5.1-5.8)	5.3 (4.7-5.9)

The results were analysed statistically using the unpaired Wilcoxon rank sum test; p < 0.05 was taken to indicate significance.

Results

The details of the patients are given in Table 1. Duration of anaesthesia was longer in the enflurane group but not significantly so.

Induction of anaesthesia occurred rapidly in both groups. Arterial blood pressure in the enflurane group decreased by 25% of pre-anaesthetic values in six patients compared to five patients who received propofol. The propofol infusion in the latter cases was reduced by up to one-third of the calculated dose, while the concentration of enflurane was also reduced. The hypotension was readily corrected by infusion of Hartmann's solution. The propofol infusion was maintained during the rest of the procedure once the cardiovascular state was steady without any alteration in the calculated dose. Mesenteric traction in three patients in the propofol group, resulted in a hypertensive response that necessitated administration of fentanyl.

Complications during induction and maintenance, the early recovery characteristics and the anaesthetists' assessment of the anaesthetic are shown in Table 2. The times to the start of spontaneous respiration, adequate respiratory exchange and tracheal extubation were all shorter in the propofol group, although the differences were not statistically significant (Table 3). The recovery times, however, were all significantly shorter in the patients who received propofol (Table 3). There were no significant differences in arterial blood gases prior to induction or 10 minutes after extubation (Table 4).

The results of analysis of the EEG power spectra are shown in Table 5. The relatively high power in the low frequency delta band in the control period reflects the sedative effects of the premedication. Beta power at 10 minutes after termination of anaesthesia was significantly higher after propofol than after enflurane, which reflects the greater degree of vigilance in these patients. This higher beta activity is also reflected in the spectral edge frequency, which was also significantly greater 10 minutes after anaesthesia in the propofol group.

One 84-year-old woman in the propofol group who underwent gastrectomy did not breathe adequately for 80 minutes after the infusion was stopped.

Discussion

This study demonstrates that maintenance of anaesthesia with a propofol infusion is a satisfactory method for prolonged abdominal surgery, with a more rapid recovery than after conventional anaesthesia with nitrous oxide and en-

Table 5. Mean EEG power spectra in the various frequency ranges (μV^2) for enflurane compared to propofol anaesthesia.

	Group 1 (enflurane) (n = 15)					Group 2 (propofol) (n = 15)				
	Delta	Theta	Alpha	Beta	SEF, Hz	Delta	Theta	Alpha	Beta	SEF, Hz
Control	16 583 (41%)	2356 (6%)	14 284 (36%)	6797 (17%)	15.2	14 318 (53%)	1647 (6%)	4828 (18%)	6 080 (23%)	18.0
After induction	20 342 (42%)	6897 (14%)	13 393 (27%)	8113 (17%)	16.7	6029 (19%)*	3854 (12%)	9979 (31%)*	12 078 (38%)*	17.3
Maintenance	15 709 (33%)	7152 (15%)	20 525 (42%)	5036 (10%)	12.8	9609 (22%)*	5509 (13%)	16 291 (37%)*	12 201 (28%)*	15.8
10 minutes after anaesthesia	4057 (6%)	10 849 (17%)	33 844 (54%)	14 042 (23%)	15.5	9072 (19%)*	2469 (5%)*	17 672 (37%)*	18 874 (40%)*	21.0*

SEF, Spectral edge frequency (Hz) (% refers to percentage of total frequency).

*p < 0.05.

flurane. The rapid recovery is due to the short elimination³ half-life ($t_{1/2\beta} = 45$ minutes) and the drug is suitable for long as well as for short procedures as reported by others.^{1,4,5} The rapidity of recovery was also confirmed by EEG monitoring, the high frequency range of which can be used as a sign of vigilance in the postoperative period.^{6,7}

It must be remembered that propofol possesses only hypnotic properties and additional analgesia is necessary when it is used by continuous infusion, even in combination with nitrous oxide. Fentanyl is a satisfactory agent in this respect. It should also be pointed out that all the procedures reported here were elective and that the doses of propofol used might have to be reduced in patients in higher ASA grades and in the presence of hypovolaemia.

References

1. KAY B, HARGREAVES J, SIVALINGHAM T, HEALY TEJ. Intravenous anaesthesia for cystoscopy: a comparison of propofol or methohexitone with alfentanil. *European Journal of Anaesthesiology* 1986; 3: 111–20.
2. STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 152–6.
3. COCKSHOTT ID. Propofol ('Diprivan') pharmacokinetics and metabolism—an overview. *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 45–50.
4. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA, STEPHENSON DK. Dose requirements of ICI 35 868 (Propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; 39: 1168–71.
5. KNELL PJW, MCKEAN JF. An investigation of the pharmacokinetic profile of propofol ('Diprivan') after administration for induction and maintenance of anaesthesia by repeat bolus doses in patients having spinal anaesthetic block. *Postgraduate Medical Journal* 1985; 61 (Suppl. 3): 60–1.
6. BOVILL JG, SEBEL PS, WAUQUIER A, ROG P. Electroencephalographic effects of sufentanil anaesthesia in man. *British Journal of Anaesthesia* 1982; 54: 45–52.
7. FREYE E, HARTUNG E, BUHL R. Alfentanil als letzte Dosis bei der Neuroleptanesthesia mit Fentanyl. *Anaesthesist* 1986; 35: 231–7.

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Effect of propofol on elevated intracranial pressure. Preliminary results

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Summary

The effects of a bolus injection of propofol on mean intracranial pressure were studied in six adult, comatose patients who had severe head injuries. Propofol 2 mg/kg was given intravenously over 90 seconds when the mean intracranial pressure reached or exceeded 25 mmHg. Arterial blood gas values, heart rate and central venous pressure remained stable at all measurements. Arterial blood pressure decreased statistically significantly ($p < 0.05$) within one minute after propofol administration. The mean (SEM) intracranial pressure decreased statistically significantly ($p < 0.05$) at 30 seconds and at 1 and 2 minutes, from 25 (3) to 11 (4) mmHg. The cerebral perfusion pressure decreased statistically significantly from 92 (8) mmHg at all measurements ($p < 0.05$). The lowest value at 3 minutes was 50 (7) mmHg but in four patients at that time the perfusion pressure was below 50 mmHg.

Key words

Anaesthetics, intravenous; propofol.
Measurement techniques; intracranial pressure.

This study reports our experience with propofol in emulsion formulation in patients with elevated intracranial pressure (> 25 mmHg). The objective was to assess the effect of a bolus injection of propofol on intracranial pressure, blood pressure, heart rate, arterial blood gases and cerebral perfusion pressure.

Methods

The study was approved by the ethical committee of the hospital. It involved six patients of both sexes aged between 22 and 57 years (mean 33, SEM 6). All suffered from severe head injuries and were unconscious, their tracheas intubated and were receiving controlled ventilation of their lungs. The decision about intraventricular pressure monitoring was made after clinical examination and computerised tomography of the brain. Blood pressure was recorded by an

invasive method once the intraventricular catheter and transducer were in place.

Propofol 2 mg/kg was given intravenously over 90 seconds provided that the haemodynamic status of the patient was stable, if the mean intracranial pressure increased to more than 25 mmHg despite adequate sedation with fentanyl and muscle relaxation with pancuronium. Arterial blood samples (PaO_2 , PaCO_2 and pH) were analysed before and 6 minutes after propofol administration. Systolic and diastolic arterial blood pressure, heart rate, central venous pressure and intracranial pressure were assessed before propofol injection and at one-minute intervals until 6 minutes later. The mean arterial pressure and cerebral perfusion pressure (mean arterial pressure – intracranial pressure) were calculated. Statistical analysis was performed by Friedman two-way analysis of variance.

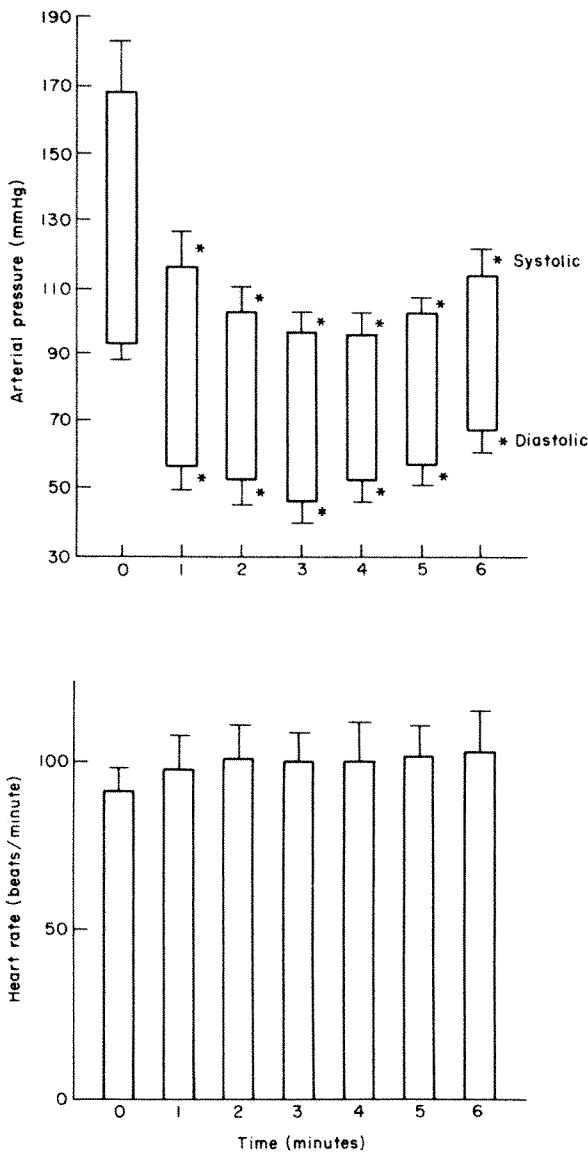


Fig. 1. Cardiovascular changes, mean (SEM). * $p < 0.05$.

Results

The cardiovascular changes are shown in Fig. 1. A statistically significant ($p < 0.05$) decrease in systolic and diastolic arterial pressures was noted one minute after propofol administration (systolic pressure, from a mean (SEM) of 168 (15) mmHg to 115 (10) mmHg; diastolic pressure, from 92 (5) mmHg to 56 (7) mmHg), as well as in mean arterial pressure (from 118 (7) mmHg to 78 (7) mmHg; $p < 0.05$). No changes in heart rate (100 beats/minute, SEM 10) were noted during the procedure. Mean arterial blood gas tensions remained stable at P_{aO_2} 14.3 (1.9) kPa and P_{aCO_2} 5.05 (0.4) kPa, and central venous pressure at 3 (1) mmHg for all measurements. The mean intracranial pressure decreased statistically significantly after 30 seconds and after 1 and 2 minutes (from 25 (3) mmHg to 11 (4) mmHg, Fig. 2). No increase in intracranial pressure was noted during the first 6 minutes after propofol administration except in one patient, where intracranial pressure regained its original value after 4 minutes. Cerebral perfusion pressure (Fig. 3) decreased statistically significantly at all measurements ($p < 0.05$), from 92 (8) mmHg to 50 (7) mmHg as the lowest value after 3 minutes. However, a cerebral perfusion pressure below 50 mmHg was noted in four patients.

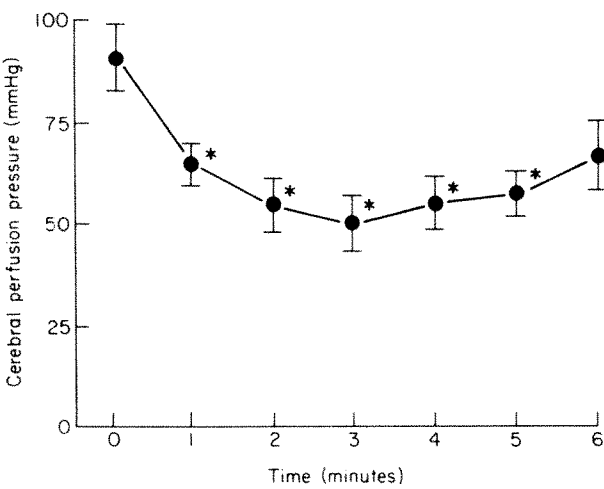


Fig. 2. Intracranial pressure changes, mean (SEM). * $p < 0.05$.

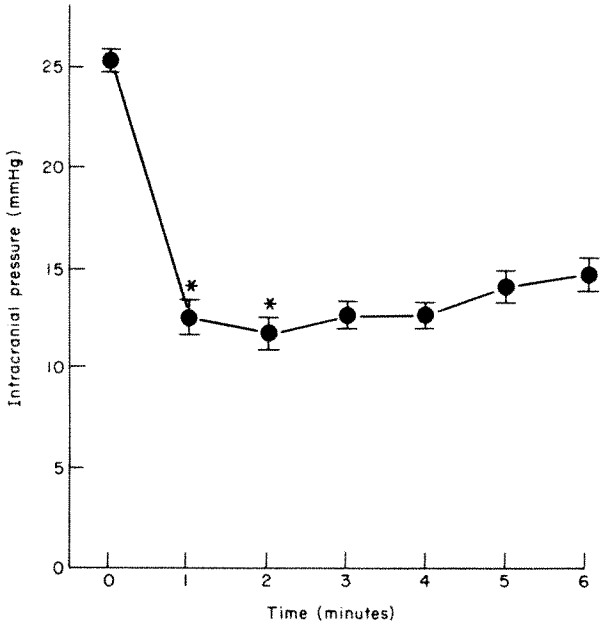


Fig. 3. Cerebral perfusion pressure changes, mean (SEM). * $p < 0.05$.

Discussion

The haemodynamic effects of propofol are comparable to previous studies. Grounds *et al.*¹ and Rolly and Versichelen² reported a statistically significant decrease in arterial blood pressure after respectively 2.5 and 2 mg/kg propofol intravenously, without changes in heart rate. Zattoni *et al.*³ and Hartung⁴ did not notice a change in mean arterial pressure after respectively 0.8 and 1 mg/kg propofol in patients who were receiving intensive care, in contrast to our results. Elevated intracranial pressure decreased after propofol administration in our study. This suggests that propofol may be used to induce general anaesthesia in patients with elevated intracranial pressure without further increase.⁴ The marked decrease in mean arterial and intracranial pressures lowered cerebral perfusion pressure, in contrast to the results of Hartung and Zattoni *et al.* Cerebral perfusion pressure decreased below 50 mmHg in four of our six patients and this value is considered to be the minimum safe perfusion pressure. Similar results were reported by Siani *et al.*⁵ who used 2.5 mg/kg propofol intravenously over 15 seconds in

uninjured, conscious neurosurgical patients who breathed spontaneously. A decrease in mean arterial and intracranial pressures caused a decrease in cerebral perfusion pressure after 1 minute.

Intracranial pressure is restored to the physiological range after administration of propofol but preservation of an adequate cerebral perfusion pressure may limit the use of the drug. Appropriate therapeutic measures are required when cerebral perfusion pressure decreases below 50 mmHg. Further investigation of single bolus requirements, injection speed or administration by continuous infusion is considered necessary before the use of propofol to decrease intracranial pressure in intensive care patients is advocated.

References

1. GROUNDS RM, TWIGLEY AJ, CARLI F, WHITWAM JG, MORGAN M. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia* 1985; **40**: 735-40.
2. ROLLY G, VERSICHELEN L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. *Anaesthesia* 1985; **40**: 945-8.
3. ZATTONI J, SIANI C, ROSSI A, CAMPORA D, BOZZO N, GUIDUCCI G, MESCOLA P. The effects of 0.8 mg/kg of 'Diprivan' and 1.6 mg/kg thiopentone on intracranial pressure and systemic blood pressure in neurosurgical patients. 3rd Italian/French Meeting of Neuroanaesthesia, SIAARTI, Capri, May 1986.
4. HARTUNG H-J. Beeinflussung des intrakraniellen Druckes durch Propofol ('Disoprivan'). *Anaesthesist* 1987; **36**: 66-8.
5. SIANI C, ZATTONI J, VERARDO T, DOLCINI G, BALESTRERO MA, SANTINI M, DELLA ROCCA M. Response of intracranial pressure and systemic haemodynamics to 0.35, 0.80 and 2.5 mg/kg i.v. 'Diprivan' in conscious and normoventilated neurosurgical patients. 3rd Italian/French Meeting of Neuroanaesthesia, SIAARTI, Capri, May 1986.

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A comparison between propofol and ketamine for anaesthesia in the elderly. Haemodynamic effects during induction and maintenance

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Summary

The haemodynamic effects of propofol and ketamine were studied in two groups of eight randomly allocated elderly patients (mean age 85.8 years) anaesthetised for hip replacement. Group 1 patients received propofol 1 mg/kg by intravenous bolus for induction and 0.1 mg/kg/minute by continuous infusion for maintenance. Group 2 patients received ketamine 1.5 mg/kg by intravenous bolus as induction dose and 50 µg/kg/minute by continuous infusion for maintenance. All patients breathed spontaneously via a facemask at F_{IO_2} 1.0. Haemodynamic status was established before induction and at 1, 3, 5, 10 and 15 minutes after induction. Arterial pressure and cardiac output decreased slightly in group 1 but heart rate, right atrial pressure and pulmonary arterial pressure remained unchanged. Myocardial oxygen consumption showed a significant decrease of 27%. There was a significant increase in blood pressure and pulmonary capillary wedge pressure (by 97%) in group 2. Cardiac output and systemic vascular resistance remained unchanged whereas myocardial oxygen consumption showed a very significant increase of 100%.

Key words

Anaesthetics, intravenous; propofol, ketamine.

This study was designed to assess the haemodynamic variations that occur during anaesthesia in elderly patients scheduled for hip replacement surgery. Ketamine is frequently used in poor risk patients because of its haemodynamic properties¹ and it was compared with propofol, a new anaesthetic agent with good pharmacokinetic properties.²

Patients and methods

Sixteen elderly patients scheduled for hip replacement, mean age 85.5 years and of ASA grade 1 or 2, were allocated randomly to one of two groups. Patients under 75 years, those with unstable coronary disease, acute cardiac failure, renal failure, obesity or adverse reactions to the drugs used were not studied.

Premedication consisted of hydroxyzine 1 mg/kg intra-

muscularly. Radial arterial cannulation for measurement of arterial blood pressure was performed under local anaesthesia. A double lumen thermodilution flotation catheter was passed into the pulmonary artery for the measurement of central venous, pulmonary artery and pulmonary artery wedge pressures. Cardiac output was determined by the thermodilution technique. All measurements were obtained in triplicate with less than 10% variations using a cardiac output computer (Edwards Laboratories 9520). An ECG and pressure monitor (ATM Cardiodigit) was attached and heart rate displayed. A 15-minute period was allowed to elapse after the attachment of the monitoring devices for stabilisation of the cardiovascular system, after which baseline measurements were obtained.

Anaesthesia in group 1 was induced with propofol 1 mg/kg injected into a freely running infusion of saline solution and maintained with 0.1 mg/kg/minute propofol given by

continuous infusion started immediately after the bolus induction dose. Anaesthesia in group 2 was induced with ketamine 1.5 mg/kg by intravenous bolus and maintained by continuous infusion of ketamine at a rate of 50 µg/kg/minute.

Cardiovascular measurements were recorded 1, 3, 5, 10 and 15 minutes after induction (time zero). Arterial blood gas tensions were measured before and 10 minutes after induction. The measurements were used to calculate cardiac index, systemic and pulmonary vascular resistances and right and left ventricular stroke work indices (RSWI, LSWI). Fentanyl 2 µg/kg was given 15 minutes after induction and tracheal intubation accomplished after muscular relaxation provided by vecuronium 0.08 mg/kg. Diastolic and systolic arterial blood pressures and heart rate were noted at 5-minute intervals during surgery. The time between the end of anaesthetic infusion and ability to open eyes was noted for each patient.

Results

Details of the two groups are summarised in Table 1; they were broadly comparable with regard to weight, age, sex and mean ASA grade. Tables 2 and 3 present cardiovascular measurements in the two groups before and at various times

Table 1. Patient data.

	Group 1 (propofol)	Group 2 (ketamine)
Mean weight, kg	51.8	52.5
Mean age, (SEM) years	86 (5.4)	85.5 (4.5)
Sex, M/F	0/8	1/7
ASA grade 1/grade 2	1/7	0/8

No significant differences between groups.

after the induction of anaesthesia. Statistical analysis (Student's *t*-test for unpaired series) showed slight significant differences between groups 1 and 2 as regards mean arterial pressure, cardiac index and LVSWI ($p < 0.05$) at control time.

Mean arterial pressure in group 1 decreased significantly by 17% ($p < 0.05$) at 1 minute and subsequently remained stable at 15% below baseline. Heart rate decreased slightly but not significantly and central venous pressure, pulmonary artery pressure and pulmonary capillary wedge pressure remained unchanged. Systemic vascular resistance and cardiac index decreased slightly and, in association with mean arterial pressure reduction, produced a significant reduction of 26% ($p < 0.001$) in LVSWI which reached a maximum 3 minutes after induction. Myocardial oxygen consumption evaluated by the triple product heart rate \times mean arterial pressure \times pulmonary capillary wedge pressure decreased significantly by 27% ($p < 0.001$) after induction and remained lower than control values.

Variations in the opposite direction were noted in group 2. Mean arterial pressure increased significantly by 10% ($p < 0.05$) 5 minutes after induction, heart rate decreased by 13% ($p < 0.05$) and cardiac index remained unchanged but pulmonary capillary wedge pressure showed a significant elevation of 97% ($p < 0.001$) after 3 minutes which produced a significant increase in LVSWI (by 20%) and in myocardial oxygen consumption (by 100%).

The variability of blood pressure during surgery is shown in Table 4 using the difference between systolic blood pressure at baseline and the value noted during surgery.

Table 5 details times between the end of infusion and opening of eyes and adequate response to a simple command. There is a difference between the two groups but previous alterations of patients' mental status reduce the validity of this test.

Table 2. Principal cardiovascular measurements in group 1 (propofol). Values expressed as mean (SEM).

	Baseline	1 minute	3 minutes	5 minutes	10 minutes	15 minutes
CVP, mmHg	2.80 (2.9)	3.12 (4.4)	2.10 (2.1)	2.80 (3.2)	2.37 (2.6)	2.87 (3.0)
PAP, mmHg	13.30 (5.6)	13.75 (3.0)	14.40 (3.6)	14.25 (4.4)	14.00 (4.8)	13.75 (3.0)
PCWP, mmHg	5.00 (4.0)	4.37 (2.7)	5.60 (2.5)	4.25 (3.6)	5.25 (3.7)	5.37 (2.4)
MAP, mmHg	96.10 (13.8)	80.62 (13.4)	82.40 (9.8)	84.37 (10.2)	81.70 (9.5)	81.12 (10.3)
HR, beats/minute	82.70 (10.6)	83.40 (14.3)	82.60 (12)	81.37 (10.6)	80.75 (10.8)	81.60 (14.5)
CI, litres/minute/sq m	3.32 (0.47)	3.10 (0.27)	2.90 (0.37)	3.02 (0.4)	3.40 (0.5)	2.99 (0.6)
SVR, mmHg/litre/minute/sq m	29.33 (4.6)	25.57 (2.8)	28.50 (3.6)	27.80 (3.6)	27.70 (4.5)	26.10 (5.8)
PVR, mmHg/litre/minute/sq m	2.60 (1.1)	2.89 (1.3)	3.08 (1.7)	3.38 (1.5)	3.05 (1.4)	2.96 (0.6)
LVSWI, g m/sq m	53.60 (8.4)	41.95 (10.2)	39.70 (2.2)	44.00 (5.5)	42.30 (6.9)	40.96 (8.5)
RVSWI, g m/sq m	5.80 (2.9)	5.98 (3.3)	6.10 (2.5)	6.01 (1.8)	6.11 (2.1)	5.70 (1.4)

CVP, Central venous pressure; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; MAP, mean arterial pressure; HR, heart rate; CI, cardiac index; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; LVSWI, left ventricular stroke work index; RVSWI, right ventricular stroke work index.

Table 3. Principal cardiovascular measurements in group 2 (ketamine). Values expressed as mean (SEM).

	Baseline	1 minute	3 minutes	5 minutes	10 minutes	15 minutes
CVP, mmHg	2.50 (2.8)	2.25 (2.4)	3.00 (2.6)	3.75 (1.7)	2.43 (2.4)	4.25 (3.8)
PAP, mmHg	22.12 (7.7)	25.87 (12.0)	27.50 (8.9)	28.00 (13.0)	27.00 (15.7)	26.00 (10.5)
PCWP, mmHg	6.50 (5.9)	10.12 (10.0)	12.62 (11.0)	10.50 (11.5)	10.50 (11.0)	10.25 (10.0)
MAP, mmHg	100.60 (18.0)	106.12 (14.0)	109.87 (17.0)	111.25 (18.0)	109.62 (14.0)	93.37 (38.0)
HR, beats/minute	97.25 (22.0)	95.62 (21.0)	93.13 (20.0)	92.62 (20.0)	91.12 (20.0)	90.00 (20.0)
CI, litres/minute/sq m	2.70 (0.6)	2.71 (0.6)	2.80 (0.6)	2.79 (0.5)	2.86 (0.5)	2.84 (0.57)
SVR, mmHg/litre/minute/sq m	38.21 (13)	40.44 (14)	40.34 (11.6)	39.90 (11)	38.70 (11)	37.34 (10)
PVR, mmHg/litre/minute/sq m	6.50 (4.6)	6.90 (4.8)	6.60 (4.1)	8.02 (7)	6.99 (7.6)	6.58 (3.8)
LVSWI, g m/sq m	37.70 (10.3)	40.45 (13.0)	42.80 (10.0)	44.50 (13.0)	45.25 (10.0)	44.64 (12.0)
RVSWI, g m/sq m	8.02 (3.1)	9.10 (4.0)	10.20 (2.7)	10.10 (5.3)	10.20 (6.1)	9.52 (3.0)

For abbreviations, see Table 2.

Table 4. Maximum decreases in systolic blood pressure during maintenance, mmHg.

Patient	Group 1 (propofol)		Group 2 (ketamine)	
	Basal	Minimum	Basal	Minimum
1	140	100	100	120
2	100	70	160	90
3	180	100	136	100
4	140	90	210	80
5	150	90	130	110
6	145	110	170	80
7	169	90	155	120
8	140	90	100	90

Table 5. Mean (SEM) recovery times.

Recovery time	Group 1 (propofol)	Group 2 (ketamine)
Eyes open, minutes	36 (55)	98 (65)
Response to command, minutes	46 (52)	166 (70)

Discussion

The cardiovascular effects of ketamine^{3,4} are well documented in adult patients. It has been shown to induce increases in mean arterial pressure and cardiac output which reach a maximum between 2 and 5 minutes after intravenous injection of a 2 mg/kg bolus dose. The effects appear to be reduced in elderly patients. A previous study⁵ showed very slight variation in these parameters but quality of recovery was very poor; these observations are confirmed in this

study. The cardiovascular effects of propofol are known in adult patients and seem to be identical in the elderly.

References

1. STEFANSSON T, WICKSTRÖM I, HALJAMÄE H. Hemodynamic and metabolic effects of ketamine anesthesia in the geriatric patient. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 371-7.
2. SCHÜTTLER J, STOECKEL H, SCHWILDEN H. Clinical pharmacokinetics of Diprivan in volunteers and surgical patients. *Anesthesiology* 1986; **65**: A555.
3. LANGREHR D. *Cardiovascular effects of ketamine: a review in ketamine and the cardiovascular system. Effects and clinical uses.* Amsterdam: Excerpta Medica, 1980: 1-15.
4. MILLER RD. Pharmacology of intravenous nonnarcotic anesthetics. In: MILLER RD, ed. *Anesthesia*. New York: Churchill Livingstone, 1981: 813-7.
5. MANEGELIA R, TOUZET M, CORSIA G *et al.* Variations hémodynamiques induites par l'anesthésie à la ketamine chez le grand vieillard. *Agressologie* 1987; **28** (in press).

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Propofol in elderly high risk patients. A comparison of haemodynamic effects with thiopentone during induction of anaesthesia

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Summary

Twenty elderly patients of ASA grade 3 or 4, received either propofol 1 mg/kg or thiopentone 2 mg/kg for induction of anaesthesia. These doses provided a convenient level of anaesthesia for all patients. There were no significant intra- or intergroup haemodynamic changes, with the exception of a decrease in diastolic pressure and rate-pressure product after propofol. It is concluded that propofol 1 mg/kg can be used to induce anaesthesia in elderly high risk patients without deleterious cardiovascular effects.

Key words

Anaesthesia; geriatric.
Anaesthetics, intravenous; propofol, thiopentone.

The use of propofol is questionable in high risk patients because of its depressant effects on cardiovascular function. It causes a greater decrease in arterial pressure at the usual doses of 2.5 or 2.0 mg/kg than thiopentone.¹⁻⁹ On the other

hand, it can be administered in patients with coronary artery disease or impaired cardiac function without deleterious effects.¹⁰⁻¹⁴ This study compared the haemodynamic effects of low doses of propofol (1 mg/kg) and thiopentone (2 mg/

kg) administered for induction of anaesthesia in elderly high risk patients (ASA grade 3 or 4) scheduled for elective general surgery.

Patients and methods

A prospective study was carried out on 20 elderly patients of ASA grade 3 or 4 scheduled for elective general surgery and allocated randomly to two groups with reference to induction agent. Local ethical committee approval was obtained for the study and oral informed consent given by all patients. Patients with a systolic pressure below 100 mmHg, those who required dopamine and those whose tracheas were already intubated, were excluded from the procedure.

Premedication was with hydroxyzine 1 mg/kg, then, one hour before operation, an 18-gauge cannula was inserted into a vein on the dorsum of the hand, a 20-gauge cannula positioned in the radial artery and a thermodilution catheter floated into the pulmonary artery via the right internal jugular vein. Cardiac output was determined by the thermodilution technique using 10 ml cold saline solution and the mean of three consecutive measurements taken. Cardiac output and pulmonary capillary wedge pressure were recorded at the end of expiration.

Baseline measurements of heart rate, systolic, diastolic and mean arterial pressures, right atrial, pulmonary artery, pulmonary capillary wedge pressures and cardiac output were made 15 minutes after the vessels were cannulated and before induction.

Anaesthesia was induced with either propofol 1 mg/kg or thiopentone 2 mg/kg given respectively at rates of 50 and 100 mg/minute. The patients breathed 100% oxygen through a facemask and ventilation of the lungs was controlled manually in apnoea. Haemodynamic data were collected 1, 3 and 5 minutes after the end of the injection of propofol or thiopentone. Thereafter, vecuronium 0.1 mg/kg was given and the last values were noted 1 minute later, before intubation.

Cardiac and systolic indices, systemic and pulmonary vascular resistances, left and right ventricular stroke work indices (LVSWI, RVSWI) and rate-pressure product were calculated by computer using standard formulae.

Data are presented as means (SEM). Statistical analysis used the Wilcoxon *t*-test for intragroup and the Mann-Whitney *U*-test for inter-group comparison. A significant difference was considered to be indicated by $p < 0.05$.

Results

The two groups were comparable with respect to age, sex, weight, height, ASA grade and site of operation (Table 1). The underlying medical problems were similar (Table 2).

Propofol and thiopentone at moderate doses caused a satisfactory level of anaesthesia in all patients. Apnoea of less than 5 minutes occurred in 50% of cases in both groups.

There were no significant variations of systolic, diastolic or mean arterial pressure within the groups (Table 3 and 4). However, the administration of propofol resulted in a transient 40% decrease of systolic arterial pressure in three patients. Propofol reduced the diastolic pressure significantly at 1, 3 and 5 minutes after induction compared to thiopentone. Rate-pressure product decreased ($p < 0.05$) at the third minute in the propofol group. There were no other statistically significant differences within or between groups in any measured or calculated haemodynamic variable at any time during the recording period.

Table 1. Details of patients

	Propofol (<i>n</i> = 10)	Thiopentone (<i>n</i> = 10)
Sex, M/F	4/6	5/5
ASA grade 4	8	7
Mean (SD) age, years	73.4 (3.7)	71.6 (2.2)
Mean (SD) weight, kg	66.6 (4.2)	70.2 (4.9)
Mean (SD) height, cm	165 (2.6)	165.3 (2)
Abdominal surgery	9	10

Table 2. Underlying medical problems

	Propofol (<i>n</i> = 10)	Thiopentone (<i>n</i> = 10)
Ischaemic heart disease	4	4
Compensated heart failure	5	3
Hypertension, hemiplegia, carotid stenosis	5	5
Respiratory insufficiency	2	3
Renal failure	3	2
Diabetes	2	1
Malnutrition	2	2
Sepsis	4	2
Disseminated cancer	2	1

Table 3. Cardiovascular data. Measured values expressed as mean (SEM)

		Baseline	1 minute after injection	3 minutes after injection	5 minutes after injection	1 minute after vecuronium
Systolic arterial pressure, mmHg	P	144 (9)	127 (13)	128 (13)	136 (12)	138 (13)
	T	147 (6)	138 (8.5)	146 (10.5)	144 (9.5)	144 (10)
Diastolic arterial pressure, mmHg	P	62 (4)	58 (5)	57 (5)	61 (6)	61 (4)
	T	74 (5)	74 (3)*	73 (5)	74 (3)*	76 (6)
Mean arterial pressure, mmHg	P	90 (5)	79 (8)	80 (7.5)	84 (7)	89 (6.5)
	T	104 (6.5)	99 (4)	97.5 (6)	98 (5)	106 (7)
Heart rate, beats/minute	P	103 (8)	96 (7.5)	94 (8)	93 (8)	94 (8)
	T	88 (5.5)	89 (6)	87 (6)	88 (9)	86 (7)
Right atrial pressure, mmHg	P	4.4 (1.4)	2.0 (1.1)	2.2 (0.9)	2.8 (1.1)	3.8 (1.2)
	T	4.6 (1.5)	2.8 (1.2)	3.5 (1.5)	2.5 (0.9)	4.9 (1.8)
Pulmonary capillary wedge pressure, mmHg	P	8.1 (1.3)	8.4 (1.1)	7.8 (1.2)	9.9 (2.2)	11.3 (1.2)
	T	9.7 (1.3)	10 (1.6)	9.4 (2.2)	9.9 (2.1)	13.2 (1.9)
Mean pulmonary pressure, mmHg	P	20 (1.6)	20.5 (1.1)	20.5 (1.1)	22.5 (2.3)	23.5 (1.9)
	T	22.2 (1.6)	25.2 (2.8)	23.5 (3.3)	22.2 (2.7)	22.8 (2.4)
Cardiac output, litres/minute	P	5.9 (0.6)	5.1 (0.4)	5.4 (0.7)	5.5 (0.7)	5.7 (0.9)
	T	5.5 (0.7)	5.7 (1.0)	5.4 (0.7)	5.2 (0.7)	4.5 (0.5)

P, propofol; T, thiopentone.

* $p < 0.05$, significant difference between groups.

Table 4. Cardiovascular data. Calculated values expressed as mean (SEM)

		Baseline	1 minute after injection	3 minutes after injection	5 minutes after injection	1 minute after vecuronium
Cardiac index,	P	3.4 (0.3)	2.9 (0.2)	3.1 (0.4)	3.2 (0.4)	3.3 (0.6)
litres/minute/sq m	T	3.0 (0.3)	3.1 (0.4)	3.0 (0.3)	2.9 (0.3)	2.5 (0.2)
Systolic index,	P	34.3 (3.0)	31.9 (2.6)	34.7 (4.0)	35.3 (4.3)	36.0 (4.9)
ml/sq m	T	35.3 (3.5)	36.1 (5.1)	35.7 (3.4)	34.8 (4.0)	30.5 (2.7)
Systemic vascular	P	1271 (134)	1282 (172)	1239 (193)	1374 (217)	1470 (268)
resistance, dyne s/cm ⁵	T	1589 (172)	1571 (155)	1523 (167)	1602 (147)	1892 (162)
Pulmonary vascular	P	168 (38)	199 (25)	212 (27)	205 (23)	207 (30)
resistance, dyne s/cm ⁵	T	204 (29)	263 (59)	218 (21)	204 (22)	187 (33)
RVSWI,	P	7.1 (1.0)	8.1 (0.9)	8.7 (1.1)	9.3 (1.4)	8.9 (1.3)
g m/sq m	T	8.3 (1.1)	10.7 (1.8)	10.0 (1.7)	9.5 (1.7)	7.4 (0.9)
LVSWI,	P	38.3 (4.6)	32.7 (5.5)	35.7 (7.0)	37.7 (6.7)	40.9 (7.5)
g m/sq m	T	46.5 (6.3)	45.0 (7.8)	43.6 (5.5)	43.0 (6.7)	38.8 (4.7)
Rate-pressure	P	14 696 (1266)	11 601 (839)	*11 378 (964)*	12 115 (1046)	12 279 (3432)
product	T	12 754 (667)	12 264 (1065)	12 814 (1473)	12 675 (1613)	12 493 (1479)

P, Propofol; T, thiopentone.

* p < 0.05, significant difference compared with baseline.

Discussion

This study confirms that propofol at a dose of 1 mg/kg induces a satisfactory level of anaesthesia in elderly patients who have severe underlying medical problems and who require major abdominal surgery. This reduced dose is advocated in the elderly.¹⁵⁻¹⁷ Adverse effects of propofol are more pronounced at doses over 1.75 mg/kg,¹⁵ which can be explained by an impairment of propofol metabolism with either a reduction of the volume of distribution or a decrease of plasma clearance.^{15,17} The incidence of apnoea is similar to that in other studies.^{4,5,8}

Propofol even at reduced doses decreases arterial pressure more than thiopentone.^{10,11,16} However, the decrease in this study involved mainly the diastolic pressure. In fact, the haemodynamic changes were less pronounced than those liable to occur in ASA grade 3^{8,16} or in patients with coronary artery disease and impaired cardiac function.⁹⁻¹⁴ Decreases in cardiac indices and arterial blood pressures in these patients are related to a significant reduction of either preload^{9,13} or afterload^{10,11,18,20} or myocardial contractility.^{12,19} These apparent contradictions can be explained by different methods of study. These include heavy premedication, different doses and injection rates of propofol, and the inclusion of other agents, especially fentanyl⁹ or nitrous oxide.¹¹

Heart rate remained unchanged in the propofol group as in most other studies,^{11,12,18} despite the decrease of arterial blood pressure. Further work is required to study this phenomenon (central vagal effect or reset of baroreflex activity). However, it causes the rate-pressure product to be reduced significantly and improves myocardial oxygen balance.

It is concluded that propofol can be used to induce anaesthesia in elderly ASA grade 3 or 4 patients without major adverse effects on cardiovascular function. However, further studies that include criteria of selection other than ASA classification, are still required to confirm this.

References

- ABRAHAM EC, GOLD MI, HERRINGTON CA. A comparison of propofol, thiopental and methohexital as induction agents. *Anesthesia and Analgesia* 1986; **65**: S2.
- MCCOLLUM JSC, DUNDEE JW. Comparison of induction characteristics of four intravenous anesthetic agents. *Anaesthesia* 1986; **41**: 995-1000.
- COATES DP, MONK CR, PRYS-ROBERTS C, TURTLE M. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anesthesia in humans. *Anesthesia and Analgesia* 1987; **66**: 64-70.
- EDELST G. A comparison of propofol and thiopentone as induction agents in outpatient surgery. *Canadian Anaesthetists' Society Journal* 1987; **34**: 110-6.
- FAHY LT, VAN MOURIK GA, UTTING JE. A comparison of the induction characteristics of thiopentone and propofol. *Anaesthesia* 1985; **40**: 939-44.
- HENRIKSSON BA, CARLSSON P, HALLEN B, HÄGERDAL M, LUNDBERG D, PONTEN J. Propofol vs thiopentone as anaesthetic agents for short operative procedures. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 63-6.
- PRYS-ROBERTS C. Haemodynamic effects of Diprivan infusion anaesthesia: comparison with other intravenous and volatile anesthetics. In: *VIIth European Congress of Anaesthesiology, Vienna, 1986. Abstracts, Vol. III*. Vienna: Verlag Wilhelm Maudrich, 1986: 296 n° 407.
- ROLLY G, VERSICHELEN L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. *Anaesthesia* 1985; **40**: 945-8.
- WILLIAMS JP, MCARTHUR JD, WALKER WE, TEUNISSEN E, RIETSEMA K, STANLEY TH. The cardiovascular effects of propofol in patients with impaired cardiac function. *Anesthesia and Analgesia* 1986; **65**: S166.
- DU GRES B, SAROUL C, GRUNER MC. Utilisation due propofol pour l'anesthésie en chirurgie cardiaque. Résultats préliminaires. *Annales Françaises d'Anesthésie et de Réanimation* 1987; **6**: 240-2.
- PATRICK MR, BLAIR IJ, FENECK RO, SEBEL PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 23-7.
- PAULIN M, JULLIAN-PAPOUN H, ROQUEBERT PO, MANELLI JC. Effets hémodynamiques du propofol utilisé comme agent unique pour l'induction. *Annales Françaises d'Anesthésie et de Réanimation* 1987; **6**: 237-9.
- PINAUD M, LEPAGE JY, JUGE C, HELIAS J, COZIAN A, SOURON R. Impact du propofol sur la fonction ventriculaire gauche du coronarien. Etudes isotopique et hémodynamique couplées. *Annales Françaises d'Anesthésie et de Réanimation* 1987; **6**: 243-6.
- STEPHAN H, SONNTAG H, SCHENK HD, KETTLER D, KHAMBATTA HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. *British Journal of Anaesthesia* 1986; **58**: 969-75.
- DUNDEE JW, ROBINSON FP, MCCOLLUM JSC, PATTERSON CC. Sensitivity to propofol in the elderly. *Anaesthesia* 1986; **41**: 482-5.
- MANEGLIA R, TOUZET M, CORSIA G, GALLAIS Y, COUSIN MT. Propofol ou kétamine pour l'anesthésie du grand vieillard. Etude des effets hémodynamiques à l'induction. *Annales Françaises d'Anesthésie et de Réanimation* 1987; **6**: 247-51.
- KIRKPATRICK T, NIMMO WS. Pharmacokinetics of propofol in elderly patients. In: *VIIth European Congress of Anaesthesiology, Vienna, 1986. Abstracts, Vol. II*. Vienna: Verlag Wilhelm Maudrich, 1986: 291 n° 454.

18. LIPPmann H, PAICIUS R, GINGERICH S, OWENS R, MOK MS, CHARNEY J, LEE TS, HARLEY D, VERESPEJ J, APPEL P. A controlled study of the hemodynamic effects of propofol vs thiopental during anesthesia induction. *Anesthesia and Analgesia* 1986; **65**: S89.
19. GROUNDS RM, TWIGLEY AJ, CARLI F, WHITWAM JG, MORGAN M. The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia* 1985; **40**: 735-740.
20. PROFETA JP, GUFFIN A, MIKULA S, DOLMAN J, KAPLAN JA. The hemodynamic effects of propofol and thiamylal sodium for induction in coronary artery surgery. *Anesthesia and Analgesia* 1987; **66**: S142.

Summaries of Other Papers and Posters

The incidence and avoidance of pain on injection with propofol

P. MUNDELEER

The use of fentanyl 2.5 µg/kg intravenously, 4 minutes before the injection of propofol significantly reduced the incidence of discomfort or pain at the site of injection in four groups of 20 patients randomly allocated to receive propofol at different rates of injection. Fentanyl with atropine also caused a significant reduction in the cardiovascular effects of tracheal intubation and a reduction in the number of supplementary bolus doses of propofol required at induction. Postoperative amnesia is brief and recovery is pleasant for most patients. Patients frequently remark that they have slept very well and have dreamt.

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Propofol and fentanyl for outpatient dental anaesthesia

S. J. SEDDON, N. ROBSON AND G. C. CORSER

Fifty-one patients who presented as day cases for apicectomy or surgical extraction of wisdom teeth were anaesthetised using propofol for induction, and maintenance with nitrous oxide, oxygen and halothane either with or without the use of fentanyl. The addition of fentanyl improved the quality of induction and intra-operative conditions, without any delay in recovery or increase in the incidence of side effects. Patients were street fit by measured performance, but still suffered from many symptoms secondary to the operative procedure.

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Comparison of propofol, methohexitone and midazolam as anaesthetic induction agents in patients undergoing otolaryngological surgery

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Propofol 2 mg/kg ($n = 30$), methohexitone 2 mg/kg ($n = 30$) and midazolam 0.34 mg/kg ($n = 27$) were compared as anaesthetic induction agents in a randomised study in adult patients of ASA grade 1 or 2 who underwent otolaryngological surgery. Their ages ranged from 28–36 years. Premedication was with pethidine 1 mg/kg and atropine 0.01 mg/kg intramuscularly about 70 minutes before the start of anaesthesia. The induction agent was given over 45 seconds into a vein in the dorsum of the hand. The mean induction time was 57 seconds in the propofol group, 52 seconds in the methohexitone group and 85 seconds in the midazolam group ($p < 0.01$ compared to the other groups). Apnoea occurred in 52–57% of the patients. The mean duration of apnoea was 12 seconds after propofol, 14 seconds after methohexitone and 26 seconds after midazolam.

The mean control values for the heart rate and systolic

and diastolic arterial pressures ranged respectively from 86–87 beats/minute, 125–130 mmHg and 77–83 mmHg between the groups. Heart rate immediately after induction of anaesthesia increased by 21% in the methohexitone group and by 1–3% in the other groups. The decrease in systolic arterial pressure ranged from 7–10% and that in diastolic arterial pressure from 1–6% between the groups. Heart rate after tracheal intubation, facilitated with suxamethonium 1 mg/kg, increased by 18% in the midazolam group and by 10% in the other groups. Systolic arterial pressure increased by 40% in all groups and diastolic arterial pressure by 50% in the methohexitone and midazolam groups. Diastolic arterial pressure in the propofol group did not change after intubation.

The mean control value for the QT interval of the ECG corrected to a rate of 60 beats/minute was 421 milliseconds in the propofol group, 451 milliseconds in the methohexitone group and 428 milliseconds in the midazolam group. The QT interval changed neither statistically nor clinically significantly after any of the induction agents. The highest value in all groups occurred after intubation; 437 milliseconds in the propofol group, 454 milliseconds in the methohexitone group and 456 milliseconds in the midazolam group. The values after intubation differed statistically significantly from the corresponding control values both in the propofol ($p < 0.01$) and in the midazolam group ($p < 0.001$). The QT interval in the propofol group, however, remained below the upper limit (440 milliseconds) of the normal range. ECG changes occurred in 3% of the patients in the propofol group and in 7–10% in the other groups.

Side effects occurred in 40–43% of the patients in the methohexitone and propofol groups and in 8% in the midazolam group ($p < 0.05$ compared with the other groups). The most common side effects in the methohexitone group were hiccough (13%), flush or rash (13%) and pain at the site of injection (3%); those in the propofol group were flush or rash (27%), pain at the site of injection (20%) and movement not related to light anaesthesia (10%). No serious side effects occurred.

The present results show that propofol did not offer any special advantages over methohexitone for induction of anaesthesia. However, propofol had a more rapid onset of action by comparison with midazolam, although it produced more side effects.

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Propofol for sedation during epidural anaesthesia

H. NOLTE AND R. DERTWINKEL

Propofol was used for sedation in 39 patients of ASA grade 1 or 2 who underwent surgery with the aid of lumbar epidural anaesthesia. Premedication consisted of either morphine or pethidine with hyoscine. Thirty minutes were allowed to elapse after injection of bupivacaine 0.75% at L_{3/4}, so that any changes in the circulation had stabilised. Propofol 1 mg/kg was then injected intravenously and followed by a continuous infusion of propofol at either 1.0,

1.5 or 2.0 mg/kg/hour. Pain on injection occurred in 26 patients; it was mild in 16 and severe in 10. Only six patients remembered the pain postoperatively. No significant changes occurred in heart rate, arterial blood pressure or respiratory rate after commencement of propofol. Dose dependent respiratory obstruction, which was easily managed by an oral or nasopharyngeal airway, occurred in 16 of the 39 patients. Recovery from sleep varied from 1 to 7 minutes and averaged just under 3 minutes; thirty-five patients described the period of sleep as pleasant. Fifteen patients complained of nausea or vomiting postoperatively.

It is concluded that propofol in a dose of 1.5 or 2.0 mg/kg/hour after a bolus of 1.0 mg/kg produces excellent sedation during epidural anaesthesia and is likely to be superior to other available drugs.

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Propofol as a sedative for inguinal hernia repair under local anaesthesia

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This study investigated the use of propofol given as a continuous infusion for sedation to supplement ilio-inguinal nerve block and infiltration of local anaesthetic for inguinal herniorrhaphy in 22 adult patients. The desired level of sedation, defined as absence of the eyelash reflex and of spontaneous movement, was achieved with acceptable cardiovascular alterations. The greatest reductions from baseline blood pressure and heart rate were 22.12% ($p < 0.0001$) and 12.34% ($p = 0.0066$), respectively. The average duration of infusion was 120 minutes 25 seconds (SD 46 minutes 35 seconds) and the mean recovery time was 6 minutes 30 seconds (SD 5 minutes 39 seconds). The mean rate of infusion was 4.86 mg/kg/hour (SD 1.55).

There were no postoperative complications and several patients commented that they felt well by comparison with their experience of general anaesthesia for minor surgery. The surgeons, anaesthetists and patients alike judged this technique to be very acceptable.

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Propofol for thoracic surgery

J. L. MOURAND, M. NEIDHARDT-AUDION, N. SCHIPMAN, M. ROUSSEL, A. NEIDHARDT, F. CLEMENT AND J. P. ETIEVENT

Good analgesia and rapid recovery of consciousness are desirable after thoracic surgery in order to minimise respiratory problems. These conditions could be met by a combination of general anaesthesia with propofol and a regional technique. Thirty-two patients were studied; in 16 of these a catheter was sited in an intercostal space at the level of the thoracotomy incision, while in the remaining 16 patients an epidural catheter was inserted into the 6th or 7th thoracic interspace. Anaesthesia was induced with propofol 2.5 mg/kg and dextromoramide 5 µg/kg after injection of 15 ml 0.5% bupivacaine in each patient, and the trachea intubated after vecuronium 0.1 mg/kg. Anaesthesia was maintained with an infusion of propofol 9 mg/kg/hour for 30 minutes reduced to 4.5 mg/kg/hour thereafter, and

relaxation with vecuronium 0.1 mg/kg/hour which was stopped after bronchial suture; the propofol infusion was stopped at the first point of cutaneous suture. Arterial blood pressure and heart rate were measured at 5-minute intervals throughout surgery. The following times were noted from cessation of the propofol infusion: extubation; recovery of psychometric performance to pre-operative values; and the best maximum minute ventilation which approximated to the value found 48 hours postoperatively.

The average duration of anaesthesia was 214 minutes in both groups. Three patients in the intercostal group developed bradycardia during induction, while the systolic arterial pressure decreased by 30% from control values in eight patients. The cardiovascular system remained stable after incision. Induction of anaesthesia in the epidural group was accompanied by bradycardia in six patients and by a decrease in systolic arterial pressure of 30% in seven patients. The time to recover all mental faculties postoperatively was 50 minutes (SD 11) in all patients. Maximum ventilation was achieved 60 minutes after the end of anaesthesia.

Awakening from anaesthesia in this study was rapid and allowed early physiotherapy. However, 50% of patients showed a decrease in arterial pressure of 30% on induction. The use of propofol combined with regional anaesthesia is a feasible method to meet the requirements of thoracic surgery in patients without cardiovascular disease.

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Total intravenous anaesthesia by infusion of propofol compared to propofol-nitrous oxide anaesthesia. Preliminary results

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Twenty patients of ASA grade 1 admitted for elective hemilaminectomy were randomly allocated to receive either total intravenous anaesthesia (group 1) or intravenous anaesthesia supplemented with nitrous oxide (group 2). Neuromuscular paralysis was with pancuronium. Both groups also received 0.003 mg/kg fentanyl and supplementary analgesia as required. Blood samples were taken for determination of s-cortisol and blood glucose before induction, 30 minutes after the start of surgery and 2 hours after surgery.

Mean blood pressures in the two groups during anaesthesia were comparable ($p > 0.05$, analysis of variance). The mean duration of infusion was 79.2 minutes in group 1 and 77.3 minutes in group 2 (NS). Total doses of fentanyl were 4.6 µg/kg in group 1 and 3.4 µg/kg in group (NS). s-cortisol 30 minutes after the start of surgery had decreased by 132 nmol/litre compared to pre-operative values in group 1 and by 89 nmol/litre in group 2 (NS). Mean s-cortisol values 2 hours after surgery in group 1 were 96 nmol/litre lower than pre-operatively whereas the mean values in group 2 had increased by 221 nmol/litre ($p < 0.05$). Blood glucose values showed almost no variation in either group. The protracted decrease in s-cortisol needs further investigation.

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Respiratory effects of a continuous infusion of propofol. A comparison with isoflurane

C. DE PAUW AND G. ROLLY

Thirty unpremedicated males scheduled to undergo arthroscopy with meniscectomy were randomly divided into two groups. One group received a bolus of propofol 2 mg/kg for induction of anaesthesia, followed by a continuous intravenous infusion of 200 µg/kg/minute for 30 minutes which was then reduced to 150 µg/kg/minute for 30 minutes. The other group received the same induction but anaesthesia was maintained with isoflurane 1.3% for 30 minutes, which was then reduced to 1%. Both groups breathed nitrous oxide by facemask.

Anaesthesia was induced successfully in all patients. Seven patients became apnoeic in the propofol group compared to six given isoflurane; the mean durations of apnoea were identical (63 seconds). Tidal volumes were markedly decreased one minute after induction; the maximum reductions were 63% and 67% in the propofol and isoflurane groups, respectively. Those who received isoflurane had greater rib cage volumes and smaller abdominal cage volumes than the propofol group. The ratio of abdominal cage volume to tidal volume remained constant in the latter patients, whereas this ratio increased by 7% in those who received isoflurane.

Paco₂ and respiratory rate increased gradually in both groups; minute volume increased to 140% of control in the propofol patients and 150% in the isoflurane group. Heart rate and arterial blood pressure increased initially, then decreased, and then remained stable with a tendency to return to pre-induction values as anaesthesia progressed. Mean awakening time was 6 minutes in the isoflurane group, which was not significantly different from the 8.5 minutes in the propofol patients. There were no major adverse reactions during or after anaesthesia.

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Total intravenous anaesthesia with propofol for laryngotracheobronchoscopic procedures

L. VERSICHELEN, G. ROLLY AND L. HERREGODS

Propofol was used for induction of anaesthesia and for maintenance by continuous infusion in 317 adult and paediatric patients (excluding neonates) who underwent ENT endoscopic procedures. Anaesthesia in an initial group of 12 adult patients was induced with 2 mg/kg propofol given within 20 seconds and maintained by continuous infusion started immediately at a rate of 12 mg/kg/hour. The propofol was preceded by an injection of alfentanil 15 µg/kg in all further adults, whereas anaesthesia in paediatric patients was induced by an inhalational technique. Anaesthesia was maintained with propofol 9 mg/kg/hour and increments of alfentanil 7 µg/kg as needed. The lungs of all patients were ventilated with an intermittent oxygen and/or air injection technique, using an AGA Bronchovent or Acutronic high frequency ventilator.

Induction of anaesthesia was smooth in all patients. Moderate to severe pain after injection of propofol in a vein on the dorsum of the hand was experienced by only a few patients (7%), although some had received alfentanil pretreatment. Nine patients of the initial group developed marked tachycardia and side effects such as sweating, lacrimation and dysrhythmias, which indicate that anaesthesia with propofol alone was too light. The addition of

alfentanil improved anaesthetic conditions. The decrease in systolic and diastolic arterial pressures after induction was statistically significant. Blood pressure increased once surgery had started but it remained below baseline values; heart rate remained stable after the initial moderate increase.

Blood propofol concentrations at the start of surgery were statistically significantly higher in the first 12 patients who received 12 mg/kg/hour propofol (5.2 µg/ml, SEM 0.3) than in 41 patients who received 9 mg/kg/hour (4.3 µg/ml, SEM 0.2). They were nearly identical at the end of surgery (3.6 µg/ml, SEM 0.2 and 3.5 µg/ml, SEM 0.2, respectively), which suggests an effect of alfentanil. The recovery times were short and there was no postoperative hangover, vomiting or nausea.

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Propofol for total intravenous anaesthesia in otorhinolaryngological surgery

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The aim of this study was to evaluate total intravenous anaesthesia by continuous infusion of propofol for ear, nose and throat surgery. Thirty-six patients premedicated with buprenorphine 0.3 mg and atropine 1.0 mg intramuscularly 45 minutes before induction were studied. Anaesthesia in all patients was induced with a bolus dose of propofol 2.5 mg/kg, their tracheas were intubated and the lungs mechanically ventilated with 100% oxygen. A continuous infusion of propofol 60–120 ml/hour was then given. Trimetaphan was administered in cases that required induced hypotension. Neuromuscular blockade was achieved with pancuronium 0.08 mg/kg when needed. The results suggest that propofol is a promising drug for total intravenous anaesthesia.

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Comparison of propofol and methohexitone for dental and maxillofacial surgery

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A prospective study was carried out to compare the anaesthetic activity of propofol, a new intravenous anaesthetic agent, and methohexitone. Forty patients of grade 1 or 2 ASA, aged 18–50 years and scheduled to undergo maxillofacial surgery, were assigned to one of two groups. All patients received standard premedication given intramuscularly.

Anaesthesia was induced after insertion of an intravenous cannula, with propofol 2 mg/kg injected over one minute or with methohexitone 3 mg/kg and fentanyl 0.86 µg/kg, and maintained with a continuous infusion of propofol 5 mg/kg/hour on methohexitone 4.5 mg/kg/hour with fentanyl 38 µg/kg/hour.

Haemodynamic variables were monitored non-invasively and breathing, anaesthesia and possible side effects were assessed. Propofol provided a better quality of anaesthesia than methohexitone during induction, maintenance and

recovery. Induction time was the same in both groups; the quality of induction and of tracheal intubation favoured propofol. Anaesthesia was more stable during maintenance and there were fewer side effects after propofol and the heart rate was slower. However, it is especially during recovery that propofol appears to be superior: recovery from propofol was more rapid with regard to all criteria considered and the time taken for complete psychomotor recovery was twice as long with methohexitone (65 minutes) as with propofol (30 minutes).

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Propofol for induction and maintenance of anaesthesia in disc herniation surgery (including preliminary results on EEG and evoked potential evaluation)

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Propofol was used for induction and maintenance of anaesthesia in 30 healthy patients who underwent surgery for disc herniation. The changes in electroencephalographic readings were similar to those after intravenous anaesthetics. Similarly, the sensory evoked potentials indicated that propofol causes a slight decrease in conduction velocity.

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Propofol infusion combined with high frequency jet ventilation for microlaryngoscopic procedures. A comparison of two dosage regimens with or without fentanyl supplementation

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Twelve patients scheduled for microlaryngoscopy were randomly allocated to receive by infusion either 12–15 mg/kg/hour propofol alone (group 1) or 6–9 mg/kg/hour with fentanyl supplementation (group 2). All patients were premedicated with oral diazepam 1 hour before the procedure and all received an induction dose of about 2 mg/kg propofol, preceded in group 2 by a bolus dose of fentanyl 1 µg/kg. Patients in group 2 received incremental doses of fentanyl as required. An insufflation catheter was placed nasotracheally and connected to a high frequency jet ventilator (Acutronic MK 1000) using 100% oxygen or 50% oxygen in air.

Hypotension was observed in both groups to a similar degree and was significant. Placement of the laryngoscope caused sustained hypertension in both groups throughout the procedure. Mean arterial pressure decreased to slightly below baseline when the laryngoscope was removed, with a gradual return to baseline on recovery. Heart rate was never significantly altered. The mean (SD) time from the end of infusion to orientation (correct recall of date of birth) was 13.2 (2.7) minutes in group 1 and 17.0 (2.0) minutes in group 2 ($p = 0.036$). The Steward score was better at 15 minutes in group 1 ($p = 0.02$), due to a rapid return to adequate ventilation.

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Propofol and radiotherapy

V. BANSSILLON AND B. MIKAELIAN

Thirty premedicated patients who underwent radiotherapy for tumours of the breast, throat, uterus or rectum received a single dose of phenoperidine 30 µg/kg in patients <6 years and 20 µg/kg in older patients before induction of anaesthesia with propofol 2.5 mg/kg in patients <60 years and 2 mg/kg in older patients. Anaesthesia was maintained by continuous infusion of propofol at a rate of 6 mg/kg/hour for a mean duration of 50 minutes (range 20–90 minutes). Induction was rapid and of good quality but was usually accompanied by a decrease in arterial blood pressure. Recovery was rapid and pleasant. The results suggest that propofol is a suitable agent for patients who undergo radiotherapy.

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The use of propofol as a total intravenous anaesthetic agent for thoracic surgery

D. L. COPPEL AND J. R. JOHNSTON

High frequency jet ventilation has made it possible to operate on certain thoracic surgical patients with greater safety. This technique requires total intravenous anaesthesia but neither Althesin nor ketamine is entirely satisfactory.

One hundred patients (70 men) scheduled for elective surgery and premedicated with morphine and atropine were admitted to the trial. An intravenous infusion of crystalloid was started before the induction of anaesthesia and fentanyl 100 µg was given prior to a sleep dose of propofol administered over 30 seconds. A propofol infusion was started at a rate up to 10 mg/kg/hour as soon as the arterial blood pressure returned to pre-induction levels. Propofol infusion was supplemented with nitrous oxide in 60 patients. Patients were classified as of ASA grades 2–4 (63% were of grade 3) with a mean age of 54.1 years and a mean weight of 66.4 kg. The average duration of surgery was 114 minutes.

Hypotension occurred on induction but arterial pressure returned to pre-induction values with tracheal intubation and remained at these levels throughout and heart rate was unchanged. The average sleep dose of propofol was 114 mg (1.75 mg/kg). The dose infused was 915 mg but was less (743 mg) in the presence of nitrous oxide. The maximum infusion rate was 69 ml/hour (10.8 mg/kg/hour) in the oxygen group and 61 ml/hour (9.2 mg/kg/hour) when nitrous oxide was used. Similarly, the minimum infusion rate in the oxygen group was 31.3 ml/hour (4.9 mg/kg/hour) and 23.8 ml/hour (3.5 mg/kg/hour) in the nitrous oxide group.

Anaesthesia was inadequate in 15 patients in the oxygen-only group and five in the nitrous oxide group. A further dose of fentanyl or a modest increase in the infusion rate was necessary to correct this. There were no instances of awareness, nausea, vomiting, delirium, dreams or hallucinations. Blood loss was unremarkable. Recovery from anaesthesia was smooth and rapid. Patients anaesthetised with oxygen–air breathed spontaneously 7.9 minutes after the end of the infusion and opened their eyes at 12.3 minutes; the times for those anaesthetised with nitrous oxide–oxygen were 10.5 and 14.8 minutes, respectively. Analgesia was required sooner in the oxygen group than in the nitrous oxide group.

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Propofol anaesthesia for ambulatory neuroradiological procedures

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Propofol was used in 25 patients (19 male) of mean age 48 years (SD 17) during neuroradiological procedures (21 carotid angiography and five CT scanning). Sixteen of the patients were uncooperative because of their neurological condition. Anaesthesia was induced after atropine 0.25–0.75 mg intravenously, with propofol 2 mg/kg followed by intermittent injections of 1 mg/kg every 7 minutes in 11 patients or by a continuous infusion of 100–150 µg/kg/minute in the remainder. Induction and subsequent maintenance of anaesthesia were satisfactory in all cases. There was a mean decrease in arterial pressure of some 12% (SD 7%). Respiratory effects were minimal. Recovery was excellent; the mean waking time was 7 minutes after the end of propofol administration, which enabled rapid transfer to the ward.

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Propofol by continuous infusion for anaesthesia in major neurosurgery

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Propofol was administered by infusion to induce and maintain anaesthesia in 20 adult patients of ASA grades 1–3 submitted for craniotomy for supra- or subtentorial tumours with intracranial hypertension (16 cases), cerebral aneurysm (three cases) and rhinorrhea following head trauma (one case). Infusion started at induction at rates of 6–12 mg/kg/hour and was supplemented during the sequence of suxamethonium, laryngoscopy and tracheal intubation with additional intravenous boluses of fentanyl 0.05 mg/25–30 kg, propofol 1.6 and 0.8 mg/kg in that order. Patients' lungs were mechanically hyperventilated (P_{aCO_2} about 4.0 kPa) during maintenance with 70% nitrous oxide in oxygen and pancuronium was used for muscle relaxation. The propofol infusion rate was adjusted to cause patterns of burst-suppression on the electroencephalogram and (or) mean arterial blood pressure of 70–75 mmHg at the beginning of the craniotomy. The first six patients received additional doses of fentanyl. Clinical, functional and blood biochemical data showed that propofol infusion is a useful and safe technique of neuroanaesthesia.

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Urological surgery in the elderly. An alternative anaesthetic technique using propofol

K. C. CLAYTON AND J. P. MILLS

Fifty patients with a mean age of 74.3 years (range 64–85) were studied. All were of ASA grade 1–2 and scheduled to undergo routine urological surgery under general anaesthesia. Hospital ethical committee approval was obtained and all patients gave informed consent.

No premedication was given and all patients were induced by slow intravenous injection of propofol until the eyelash reflex was obtunded. Anaesthesia was then maintained with incremental doses of propofol 20–30 mg on the basis of clinical judgment. Fourteen patients were given an increment of alfentanil 100 µg during surgery and three were given nitrous oxide and oxygen. The following observations were made: time to loss of eyelash reflex; time to open eyes on command at the end of surgery; time to give correct date of birth; and time to sit and walk on the ward. Arterial blood pressure and heart rate were monitored throughout. The timing and dosage of increments of propofol were noted and any significant events during induction, maintenance and recovery were documented.

Anaesthesia was induced smoothly in all patients. Movement not related to light anaesthesia occurred in six patients and three patients complained of pain on injection at induction. Mean induction time was 75.1 seconds (range 40–110) with a mean induction dose of 2.5 mg/kg (range 1.1–3.5). Mean arterial pressure decreased by an average of 13.6% at 2 minutes after induction. The mean systolic pressure decrease was 29.5 mmHg compared with 18.6 mmHg for the diastolic. Heart rate decreased by an average of 4.3 beats/minute in 20 patients, increased by 8.9 beats/minute in 25 patients and was unchanged in the other five. Relevant times in minutes (range) from the last dosage of propofol were as follows: opening of eyes, 7.4 (1.4–13.3); date of birth, 8.5 (2.2–15.9); sitting, 36.1 (10.0–95.0); walking, 81.4 (25.0–150.0).

Smooth anaesthesia was achieved in all patients and only one patient required ventilatory support. The decrease in mean arterial pressure 2 minutes after induction was not accompanied by any ECG changes or any marked increase in heart rate. Both eye opening and date of birth times were longer than figures quoted in earlier studies in younger patients and other work has suggested that the metabolism of propofol is impaired in the elderly. Nausea occurred in one patient and was probably related to the alfentanil given peroperatively. All patients received oral fluids within an hour of return to the ward, without sequelae. There was no incidence of awareness during anaesthesia.

This has been shown to be a safe and efficient anaesthetic technique in a group of patients who are often subjected to repeat procedures. We consider that it is a viable alternative given the present problems of repeat halothane anaesthesia.

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Dose requirements of propofol by infusion for transurethral prostatic resection in the elderly

X. MOREAU, J. C. GRANRY, J. P. JACOB, A. DELHUMEAU AND M. CAVELLAT

Anaesthesia was provided for transurethral resection of the prostate by an infusion of propofol in 30 patients and by methohexitone in 10 patients; all also received nitrous oxide. The propofol patients were divided into three groups of 10 and anaesthesia was induced with propofol 1.5 mg/kg in each. Anaesthesia in one group was provided with propofol alone at a mean infusion rate of 147 µg/kg/minute (SEM 40) but was judged to be unsatisfactory in four of the 10 cases. Fentanyl 1.5 µg/kg was given in another 10 patients just prior to induction and the mean infusion rate decreased to 110 µg/kg/minute (SD 37), which was not

significantly different; anaesthesia was unsatisfactory in two of the patients. The infusion rate of propofol decreased significantly to 69 $\mu\text{g/kg/minute}$ (SD 9) after fentanyl 2 $\mu\text{g/kg}$ and vecuronium 0.1 mg/kg to facilitate tracheal intubation and mechanical ventilation. Anaesthesia was assessed as excellent in all cases. Operating conditions were satisfactory in only half the patients who received methohexitone. Recovery times in the propofol patients were significantly shorter than after methohexitone.

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Effect of equipotent doses of propofol and thiopentone on blood pressure and heart rate at induction of anaesthesia. A comparison between young and old patients

G. L. SCHEEPSTRA AND L.H.D.J. BOOIJ

The effects of propofol and thiopentone on blood pressure and heart rate at induction were compared in 28 unpremedicated patients aged 25–40 years and in 29 aged 65–80 years. Anaesthesia was induced with propofol 1.5 mg/kg in 18 young and 19 elderly patients followed by continuous infusion at a rate of 9 mg/kg/hour, and with thiopentone 2.5 mg/kg in 10 young and 10 elderly patients followed by an infusion of thiopentone 6 mg/kg/hour. Additional bolus doses of propofol 20 mg or thiopentone 25 mg were given when required to induce anaesthesia. All patients received fentanyl 1.5 $\mu\text{g/kg}$ and vecuronium 0.1 mg/kg.

Baseline haemodynamic values were similar for both young and both elderly groups. Heart rate increased significantly ($p < 0.05$) immediately and 3 minutes after tracheal intubation in younger patients given thiopentone compared with those who received propofol. The decrease in mean arterial pressure before intubation was similar in both elderly groups and slightly more pronounced in young patients who received propofol than thiopentone. The increases in mean arterial pressure immediately and 3 minutes after intubation were significantly higher ($p < 0.01$) in both thiopentone groups, where the rate-pressure product was also significantly higher.

It is concluded that propofol provides more favourable cardiovascular conditions than thiopentone, especially in the elderly.

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Continuous intravenous anaesthesia with propofol and alfentanil

R. P. H. DUNNILL

Thirty-three patients with a mean age of 62 years (SD 14.6) and mean weight 71 kg (SD 12) scheduled to undergo peripheral arterial or venous surgery were premedicated with either lorazepam and prochlorperazine or papaveretum and hyoscine. Anaesthesia was induced by intravenous injection of propofol (mean dose 1.7 mg/kg) and alfentanil (3.5 $\mu\text{g/kg}$) and the trachea intubated after suxamethonium 1 mg/kg. Anaesthesia was maintained with a continuous infusion of propofol 6 mg/kg/hour and alfentanil 12.5 $\mu\text{g/kg/hour}$ for 10 minutes; the rates thereafter were reduced according to patients' needs. The infusions were stopped 10 minutes before the end of surgery. All patients breathed 67% nitrous oxide in oxygen.

There was a decrease in systolic arterial pressure and a slowing of the heart rate during induction. Depth of anaesthesia and its control were satisfactory. The mean duration of infusion was 99 minutes (SD 38); the mean infusion rate of propofol was 4.6 mg/kg/hour and of alfentanil, 9.6 $\mu\text{g/kg/hour}$. Patients over 60 years of age required significantly less propofol (4.0 versus 5.8 mg/kg/hour). Movement that required bolus doses of propofol and alfentanil occurred in 11 patients. Bradycardia (< 55 beats/minute) that required atropine occurred in 14 patients, while eight patients became apnoeic for periods of 30–45 seconds during maintenance. Severe hypotension that necessitated intravenous fluids and adrenaline occurred in one patient.

The mean time from the end of the infusion until patients opened their eyes was 19 minutes (SD 8) and until orientation, 28 minutes (SD 14). No patient vomited during the recovery period; analgesia was required between 2 and 4 hours postoperatively. The patient who developed severe hypotension was confused for the first 30 minutes postoperatively but subsequently made a good recovery. No patient reported awareness and all would have the same anaesthetic again.

R.P.H. Dunnill, Department of Anaesthetics, Royal Victoria Hospital, Bournemouth.

Propofol infusion in morbidly obese patients

J. H. J. H. HELMERS, R. J. KRAAIJENHAGEN, L. VAN LEEUWEN, AND W. W. A. ZUURMOND

Twenty morbidly obese patients (body mass index > 30) scheduled for general and orthopaedic surgery and premedicated with lorazepam 0.02 mg/kg, were anaesthetised with propofol 1.5 mg/kg after prior injection of alfentanil 1 mg (group A). Anaesthesia was maintained with propofol 8 mg/kg for the first 20 minutes and 4 mg/kg thereafter and stopped with skin closure. Analgesia was provided with alfentanil and muscle relaxation with atracurium. The patients' lungs were mechanically ventilated with an air-oxygen mixture with Fio_2 0.3. A comparison was made with 20 normal patients anaesthetised similarly (group B).

Recovery times were recorded as the time from when the pump was stopped until extubation, 14 minutes (SEM 10) in group A, 10 minutes (SEM 6) in group B (not significant); the time from the pump was stopped until the eyes opened, 14 minutes (SEM 10) in group A, 10 minutes (SEM 7) in group B (not significant); and the time from the end of surgery until full orientation (defined by ability to answer four questions correctly), 18 minutes (SEM 10) in group A, 13 minutes (SEM 7) in group B ($p < 0.05$).

All patients reported a pleasant anaesthesia although two patients in each group were nauseated and two patients in group B responded with nodding to questions during infusion but had no recall of the event. Recovery to the state of orientation was slightly prolonged in the obese group (the duration of infusion was approximately twice that in the normal group) but this was not clinically relevant.

We conclude that propofol can be safely used as the hypnotic agent in a total intravenous technique in morbidly obese patients for a duration of at least one hour of surgery.

J.H.J.H. Helmers, MD, R.J. Kraaijenhagen, MD, Hospital De Lichtenberg, Utrechtseweg 160, 3818 ES Amersfoort, L. van Leeuwen, MD, W.W.A. Zuurmond, MD, Academic Medical Centre, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.

Safety of propofol in malignant hyperthermia. Preliminary results

M. P. VERBURG AND P. M. R. M. DE GROOT

Muscle biopsies of three patients were examined according to the protocol of the European Malignant Hyperthermia Group. Propofol 100 µg/ml was found to increase the static caffeine threshold from 4 to 8 mmol/litre. No conclusion may be drawn since the patients were normal subjects but the results suggest that propofol may be used in patients susceptible to malignant hyperthermia.

M.P. Verburg, MD, PhD, Department of Anaesthesiology, De Wever Hospital, PO Box 4446, 6401 CX Herlen, P.M.R.M. de Groot, MD, PhD, Institute for Anaesthesiology, Catholic University, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.

Propofol compared with thiopentone in young and elderly patients

P. A. NIELSEN, W. SCHNEDLER AND J. H. CHRISTENSEN

Anaesthesia was induced with either propofol or thiopentone in 40 patients aged 20–40 years and in 39 patients aged 60–80 years. No premedication was given. The mean induction dose of propofol was 3.2 mg/kg in young patients ($n = 20$) and 2.1 mg/kg in elderly patients ($n = 20$). The maximum decrease in mean arterial pressure was 58.1% in patients induced with propofol and 36.4% in those who received thiopentone. A similar decrease in mean arterial pressure occurred in young and elderly patients.

P.A. Nielsen, MD, H. Schnedler, MD, J.H. Christensen, MD, Department of Anaesthesia, University Hospital, DK 8000 Aarhus, Denmark.

Comparison of propofol and isoflurane for maintenance of anaesthesia in ASA grade 3 and 4 patients

J. BUSSE, S. VON BULOW, A. KENTGENS AND R. HEIDRICH

Propofol and isoflurane were compared as anaesthetic agents in 40 patients of ASA grade 3 or 4, aged 55–90 years, who underwent prolonged abdominal surgery. Premedication was with flunitrazepam 1–3 mg orally one hour pre-operatively. Anaesthesia was induced in the propofol group with propofol 1 mg/kg and maintained with an infusion initially at a rate of 100 µg/kg/minute which was reduced if necessary. Anaesthesia in the isoflurane group was induced with thiopentone 3–5 mg/kg and the concentration of isoflurane for maintenance varied between 0.5 and 1.0%. All patients received nitrous oxide in oxygen 2:1; fentanyl was given for analgesia and vecuronium for muscular relaxation.

Cardiovascular stability was a feature of propofol anaesthesia, in contrast to other reports, and circulatory effects that required treatment were seen more frequently in those who received isoflurane. Bradycardia occurred in one patient who received propofol, while movement occurred in two. Most patients were transferred to the intensive care unit postoperatively. One patient in the propofol group was anaesthetised for 11 hours but tracheal extubation was possible a short time after the end of the infusion and full orientation returned rapidly.

It is concluded that prolonged anaesthesia with propofol in these patients did not differ markedly from the more conventional technique using isoflurane. Side effects were few and the recovery characteristics impressive.

J. Busse, S. von Bulow, A. Kentgens, R. Heidrich, Institute for Anaesthesiology, City Hospital, Solingen, Federal Republic of Germany.

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The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224–5.

BOOKS AND OTHER MONOGRAPHS

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OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

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American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

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Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10: Data from the National Health Survey, No. 69*) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

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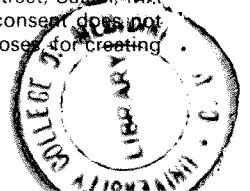
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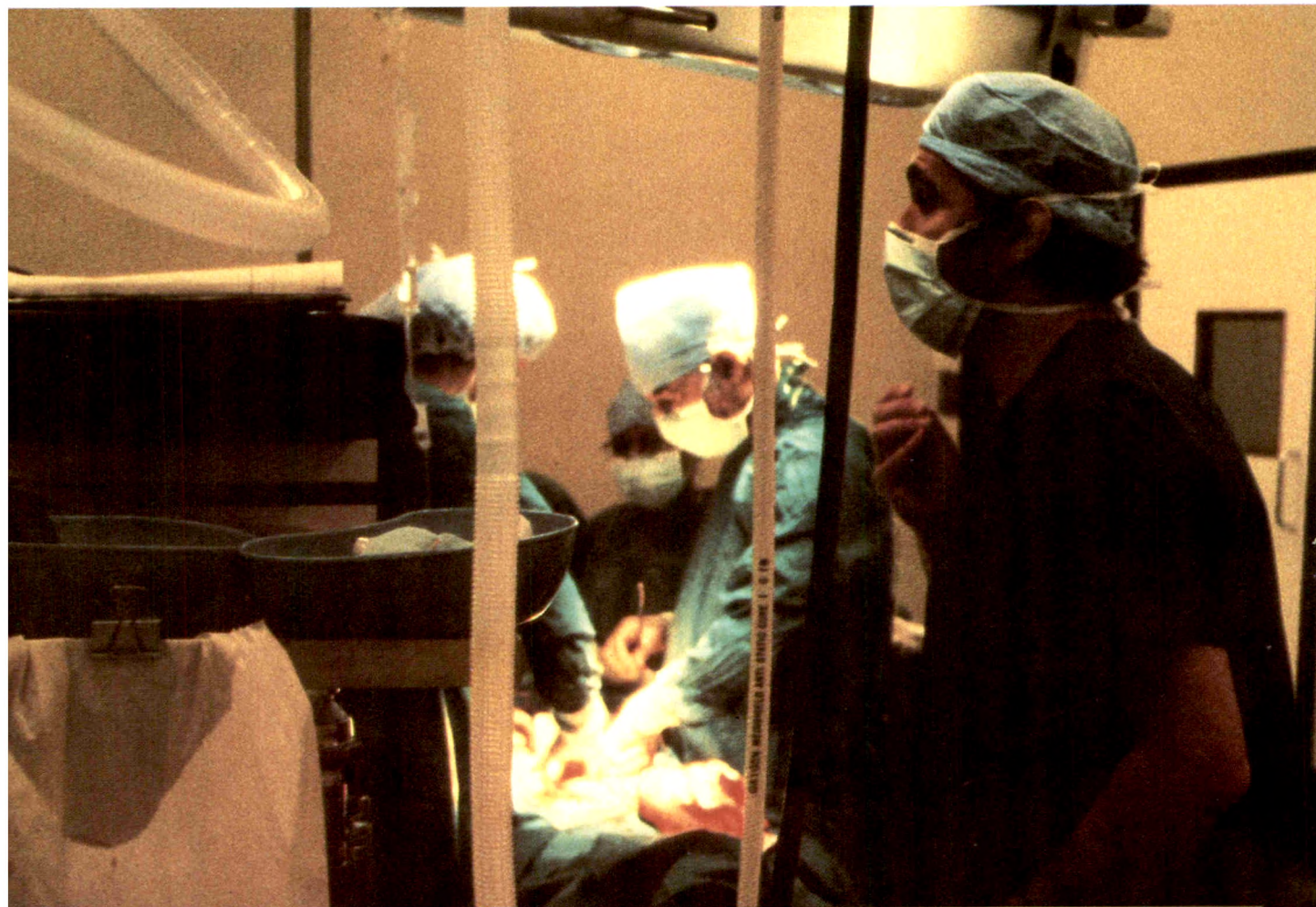
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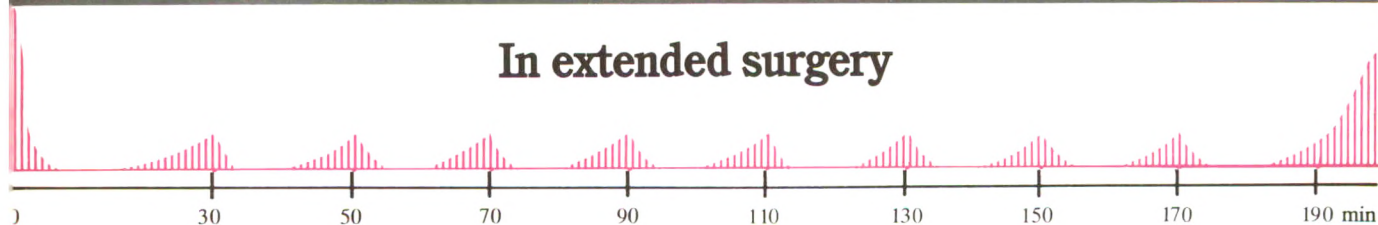
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2. Yate, P.M. *et al.* (1986), *Br. J. Anaesth.*, **58**, 112 S.

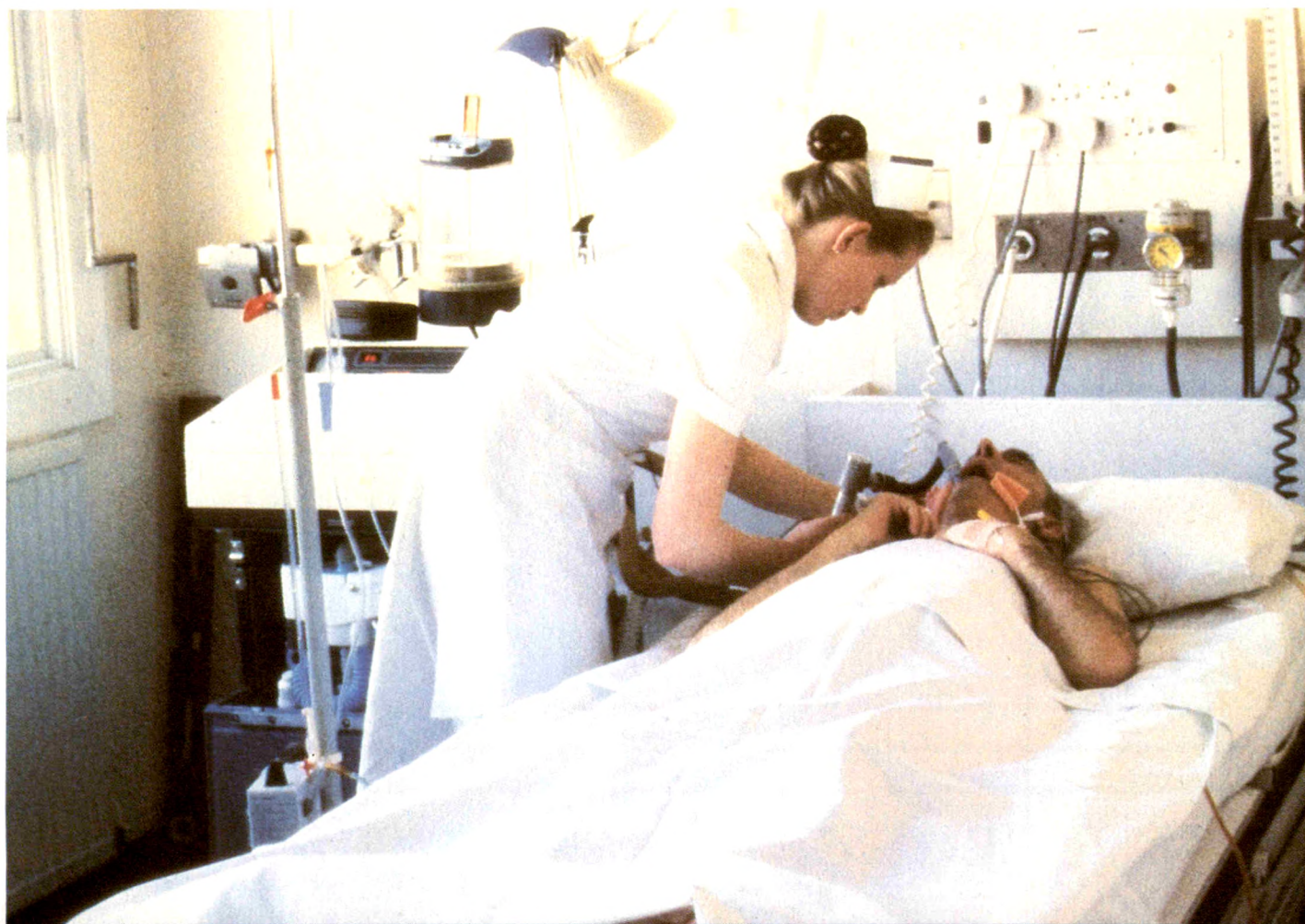
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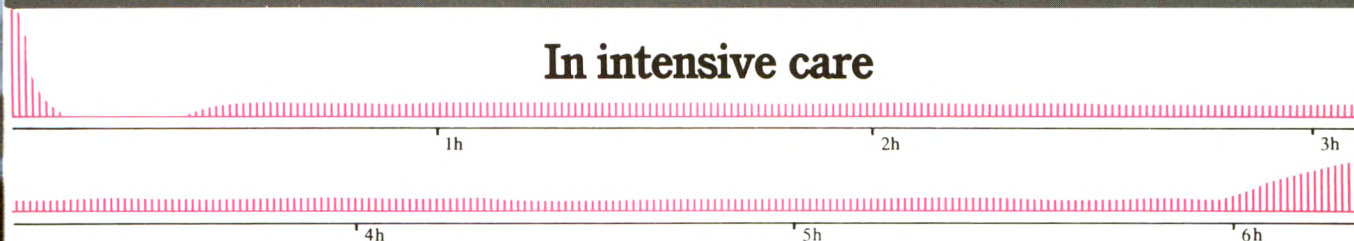


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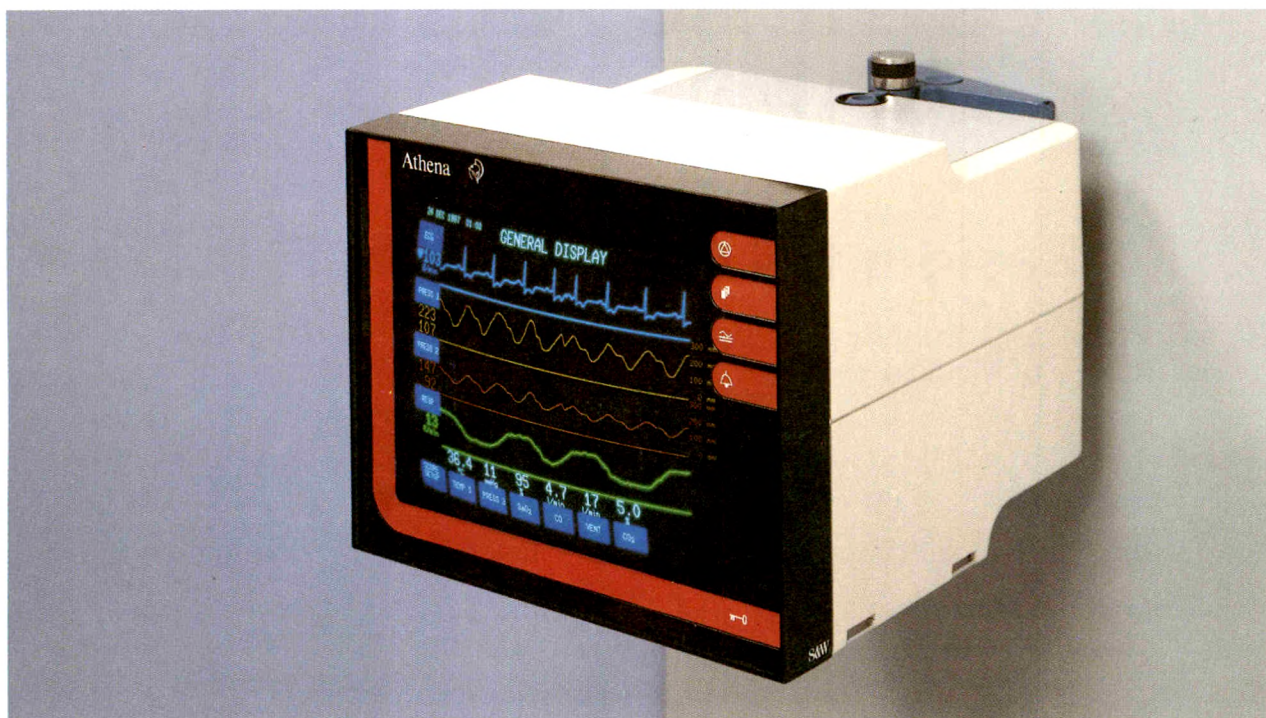
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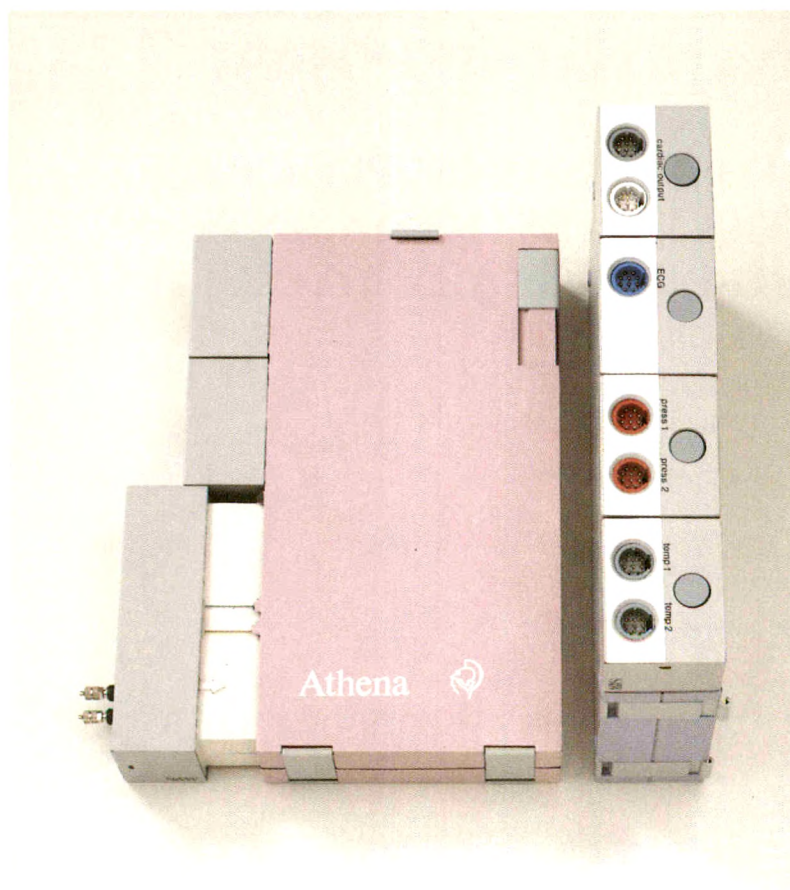
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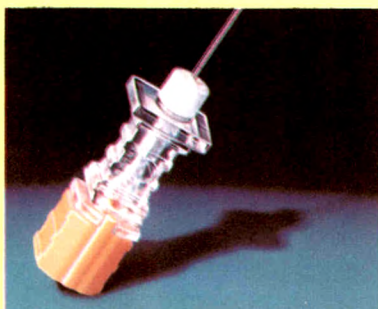
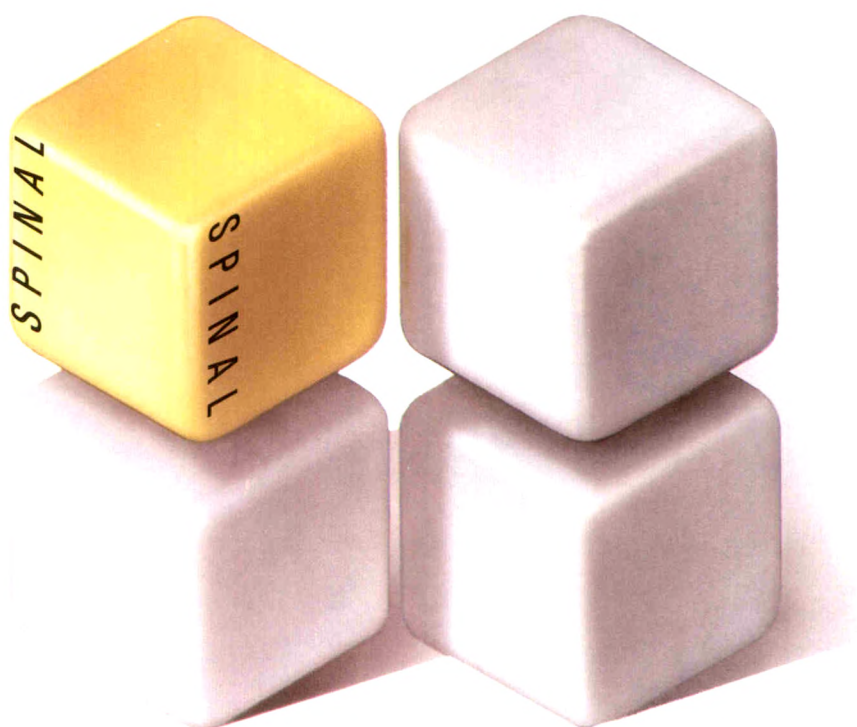
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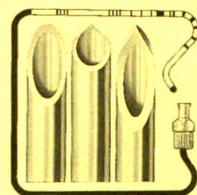
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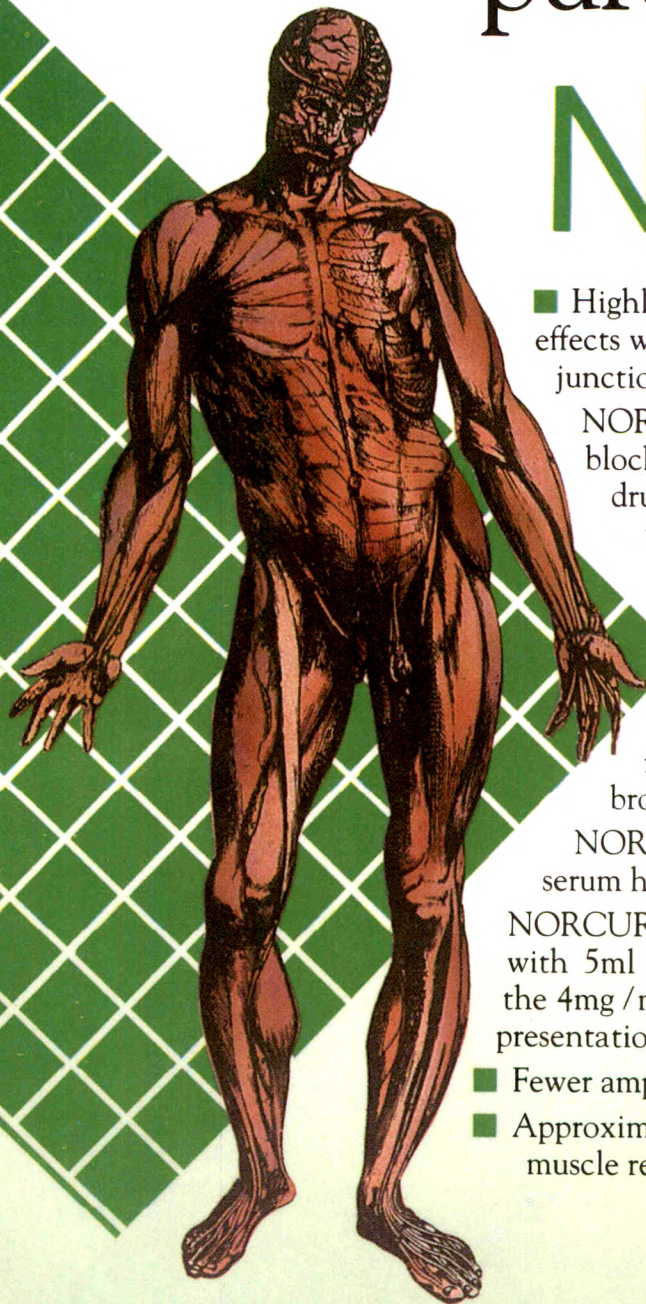
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1. Feldman SA; Clinical Experiences with Norcuron, Excerpta Medica (1983) 199-200
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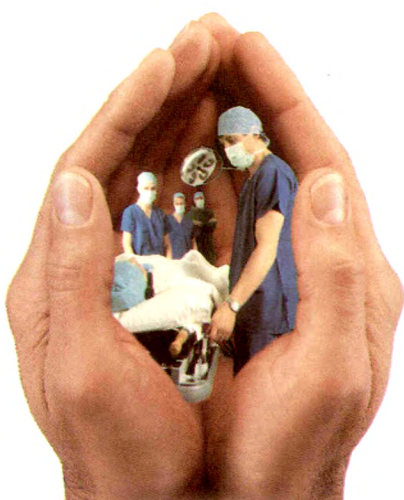
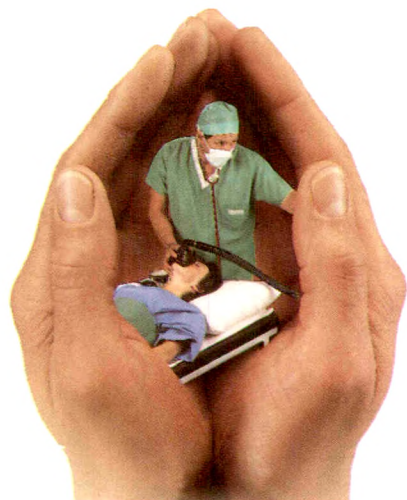
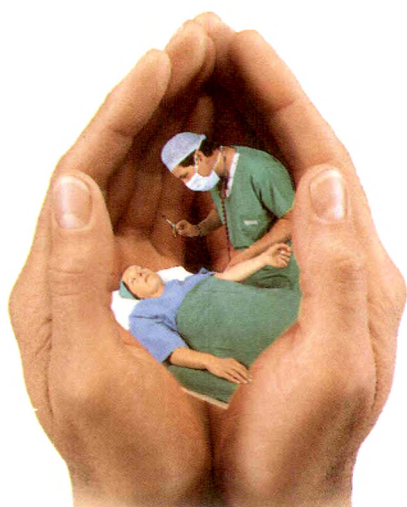
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Editorial

Consent and the anaesthetist

'Getting a patient to sign the consent form' is not at all the same thing as obtaining a real consent to the procedure which is recommended. The English law of consent when applied to medical practice embraces two quite separate concepts: assault/battery and negligence.

A procedure, such as an injection or epidural for pain relief, which is carried out without the consent of a patient may give rise to criminal proceedings for assault/battery or to civil proceedings for trespass to the person or both. There is an exception in the case of genuine emergencies. Otherwise the consent of the patient is necessary to afford adequate defence against legal proceedings. A signature on a consent form is a useful piece of documentary evidence that consent was indeed given.

However, also relevant to a consideration of consent for medical treatment is the law of negligence. A signature on a consent form is of very limited value in defending allegations of negligent counselling. This was well illustrated in the case of *Wells v. Surrey Area Health Authority*.¹

In this case a woman aged 36 years with three children developed breech presentation, maternal distress and prolonged labour in her fourth pregnancy. The locum consultant recommended emergency Caesarean section and also offered, at the same time, to perform a sterilisation. The woman signed a consent form. Her husband, who was seen later, agreed to the procedures, not least because he had been informed that his wife had signed the consent form. It was known by the obstetric team that the woman was a Roman Catholic.

After the safe delivery of the fourth child, the mother alleged that the sterilisation (but not the Caesarean section) had been performed without her consent. She alleged that she was exhausted by the labour and that she would never have agreed to the procedure had she properly understood what was intended. She commenced, through her lawyers, legal proceedings in the High Court, bringing not only allegations of negligent counselling but also of assault and battery. The Judge rejected her claim in battery after a lengthy trial and found that her signature on the consent form was an adequate defence. However, the Judge ruled that the sterilisation had not been urgently necessary and the woman had not been adequately counselled. He ruled that there had been negligence in the counselling for which he awarded compensation.

This case illustrates that there is more to consent than getting a patient's signature upon a consent form. For consent to be legally valid, the doctor is required to provide sufficient details and information about what is proposed to enable the patient to form a proper decision and to give a real consent. The extent of the explanation which the doctor should give when seeking consent will depend on many factors and may pose problems calling for fine clinical judgment. Age, maturity, physical and mental state, intellectual capacity, standard of education and the reason for the procedure, operation or treatment, are among the factors to be considered. A routine, elective procedure may need to be discussed more extensively than an emergency procedure for a life threatening condition. The explanation which must be offered by doctor to patient will also depend upon questions posed by the patient; some patients require to know far more than others about side effects or complications.

English law does not require that every possible complication and side effect should be explained to every patient.² English law permits clinicians to exercise clinical judgment in deciding how much information to pass on to patients and recognises that a balance must be struck between telling patients sufficient to enable them to give a real consent and yet not so much as to frighten them needlessly from agreeing to treatment which is demonstrably essential to their wellbeing. Achieving the balance can be difficult, requiring fine clinical judgment.

In cases of genuine emergency, practitioners may safely proceed to do what is reasonably necessary: medical and not legal considerations are acknowledged by doctors and lawyers alike to take precedence in life-threatening situations.³ However, doctors should do only that which is immediately necessary for the patient's wellbeing; coincidental and nonurgent problems which are encountered in the course of treating an emergency should not be dealt with until later, after real consent has been obtained.⁴

The principles of the law of consent under English law were reaffirmed in the case of *Sidaway v. Bethlem Royal Hospital Governors*.⁵ The House of Lords affirmed that a decision about what degree of disclosure of risks is best calculated to assist a particular patient to make a rational choice as to whether or not to undergo a particular treatment must primarily be a matter of clinical judgment. However, if there is a conflict of medical expert evidence as to whether a responsible body of medical opinion approves of non-disclosure of risks in a particular case, the trial Judge would have to resolve the conflict. In short, the doctor must decide what information should be given to the patient and in what terms that information should be couched, but his or her discretion is always subject to challenge and to scrutiny by the courts.

In cases such as *Chatterton v. Gerson*⁶ the English judiciary have made plain that plaintiffs' litigation against medical practitioners should not be founded on allegations of battery. Actions which are essentially based upon allegations of negligent counselling should allege negligence and it is important to acknowledge the limited benefits of the consent form in the defence of such litigation. Of greater value by far is evidence (preferably supported by a contemporaneous written

clinical record) that an adequate factual explanation was offered to the patient about the proposed procedure before consent was obtained. It may be helpful if verbal explanations are supplemented by a written note or leaflet, but it is most important to recognise that it is the explanation, or the lack of it, which will influence decisions about the defensibility of a claim which alleges a negligent lack of counselling amounting to a lack of real consent.

A legally-valid consent for treatment or investigations may be expressed or implied, oral or written. There is no absolute requirement for consent to be given in writing but a written consent form is helpful in providing some documentary evidence of the patient's agreement to the treatment. The problem, for defence lawyers and Health Authorities, is a practical one: disputes about consent may arise months or years after the event, by which time memories of oral explanations offered and the oral response of the patient are unreliable. A signed consent may therefore be helpful for purely evidential reasons.

However, there is no 'magic' in a consent form. It simply documents that consent was sought and obtained. However consent is obtained, the paramount consideration is that care should be taken to explain the intention, nature and purpose of what is proposed so that the patient truly comprehends that for which agreement is sought. In cases of technical complexity it is wise for a senior clinician to offer the explanation and to obtain the consent, and undesirable for this to be delegated to junior staff or, worse still, to members of the nursing profession.

So-called 'blanket' consent forms, signed at the outset of pregnancy and agreeing to 'anything that may be necessary' are of extremely limited value – indeed many would argue that they are worthless. Whilst they might, arguably, afford a small degree of protection against actions framed in battery, it has to be acknowledged that such actions are extremely rare because judicially discouraged; they would be of almost no value in defeating allegations of negligence based upon a lack of adequate advice and counselling and thus a lack of real consent to the recommended procedure.

It is important to appreciate that 'Informed Consent' has a very special meaning in certain jurisdictions within North America from the meaning given to the term informed consent in English law. To avoid confusion, the term is best avoided unless the intended meaning is clearly defined. The transatlantic doctrine of 'Informed Consent', as summarised by Lord Scarman in the *Sidaway* (*vide supra*) decision,⁵ embraces an objective test, applied by the courts, based upon what the prudent patient (i.e. not the patient one is treating) would expect to be informed about by the attending clinician.

Pace Dr. Crawford (page 335), law, like medicine, is subject to development, refinement and change. What might have been acceptable a few years ago may no longer be acceptable, not least because of the shift in professional clinical opinion which must necessarily be taken into consideration by the judiciary in the application of the 'Bolam'² (the 'reasonable practitioner') principle.

Litigation is best avoided. Good, effective communication with patients so that they understand what is being asked of them and done to them will make it less likely that they will be in that frame of mind which may spark a complaint or claim for compensation. If, however, prevention has failed and 'treatment' becomes necessary, the success or failure of the defence of a claim for compensation will, in large measure, depend upon the weight and quality of evidence given by the parties in the case. It is the oft-stated experience of the protection and defence organisations that a lack of contemporaneous notes makes a claim difficult, if not impossible, to defend especially in circumstances where, as in the Wells case, the patient's recall and her evidence is persuasive.

In applying these principles to the practice of epidural anaesthesia, a distinction is necessary between emergency and elective procedures. In the case of elective procedures an explanation should be provided so that a real understanding is achieved. It has been the experience of The Medical Protection Society, from cases referred because of complaints and claims for compensation, that patients expect to be pain free during Caesarean section under epidural analgesia. Patients may have unrealistically high expectations of the benefits of epidural analgesia and be unaware of the associated recognised complications. It would be wise for the epiduralist to explain the limits of the procedure and to warn that pain relief may not be achieved even in the best hands despite a faultless technique, and that a general anaesthetic may be necessary.

The general legal principles apply to all practitioners, whatever their special interests or discipline, and to all procedures (epidurals not excluded). Times and patients' expectations, like law and medicine, change. Queen Victoria's views about obstetric analgesia are not universally endorsed today! Pain relief is not necessarily seen as a favour graciously bestowed but may be regarded as an entitlement, to be administered faultlessly. It is important to take all reasonable steps to try to ensure that patient expectation is matched to reality.

R.N. PALMER
Deputy Secretary,

Medical Protection Society,
50 Hallam Street,
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References

1. *Annual Report 1979*. Medical Protection Society. No 87. p. 25.
2. *Bolam v. Friern Hospital Management Committee*. *All England Reports* 1957; 2: 118.
3. *Marshall v. Curry*. *Dominion Law Reports* 1933; 3: 260.
4. *Murray v. McMurchy*. *Dominion Law Reports* 1949; 2: 442.
5. *Sidaway v. Bethlem Royal Hospital Governors*. *All England Reports* 1985; 1: 643. HL.
6. *Chatterton v. Gerson*. *All England Reports* 1981; 1: 257.

Anxiety and informed consent

Does anxiety influence consent for inclusion in a study of anxiolytic premedication?

J. H. L. ANTROBUS

Summary

Forty-three consecutive patients were interviewed on the eve of elective gynaecological surgery to determine the effect of anxiety on the granting of informed consent to participate in an hypothetical study. Anxiety was assessed using the Spielberger state-trait anxiety inventory and 10-cm linear analogue scale. A standardised explanation of an hypothetical premedication study was given and the patients' consent requested. Results were grouped for those who granted ($n = 33$) and those who withheld ($n = 10$) consent: anxiety scores for the latter were significantly higher ($p < 0.01$). It is concluded that patients with high pre-operative anxiety levels are more likely to withhold consent for inclusion in premedication studies than are those who are less anxious. Seeking informed consent would introduce bias into studies of anxiolytic premedication.

Key words

Medicolegal; consent.

Ethical considerations require that a subject be informed adequately prior to inclusion in a clinical trial; it is also usual to obtain consent to such inclusion. Sample selection will be biased if the variable under investigation influences the subject to withhold that consent. Studies of the efficacy of pre-anaesthetic medication largely concern anxiolysis so it is important to determine whether anxiety can influence the granting of informed consent. This study compared anxiety levels in patients who granted permission with those who withheld consent for inclusion in an hypothetical premedication study.

Methods

Forty-eight consecutive inpatients who presented for elective gynaecological surgery were studied with the approval of the local ethical committee. They were asked to complete two assessments of anxiety, Spielberger's state-trait anxiety inventory (STAI)¹ and a 10-cm linear analogue scale.² Form Y-1 of the STAI is a self-evaluation questionnaire which estimates situational anxiety on the basis of responses to 20 statements. One of four graded responses is chosen for each statement, which generates a score from 20 (low anxiety) to 80 (high anxiety). The 10-cm linear analogue scale was fixed at the lower, left-hand end by the phrase, 'I do not feel anxious at all' and at the higher, right-

hand end by the phrase, 'I could not feel more anxious'. Anxiety levels were indicated by a vertical mark that crossed this scale and were measured in millimetres from the left-hand end.

All interviews were conducted by the author on the eve of the planned surgery. Fifteen interviews were completed before the collection of data commenced, in order to develop and rehearse a consistent approach. Forms that combined the STAI and linear analogue scale were distributed with an explanation that their purpose was to study how people felt before an operation; sufficient time was allowed for their completion. A description of an hypothetical research project was given on collection of the completed forms, before the results were examined. It was stated that two premedicant drugs were to be compared, both of which were known to relieve anxiety, in order to determine which was the more effective. Consent for inclusion in such a study was then requested, and whether consent was granted or withheld was noted.

Two groups were formed according to whether consent was granted or withheld, and compared for anxiety scores and age using Wilcoxon's two-sample rank sum test, and for the nature of the planned surgery using the Chi-square test. The STAI scores were compared with normative data for working American female adults.¹ The two methods of anxiety assessment were compared using the Pearson product-moment correlation coefficient.

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Results

Only the results from 43 women are presented since four patients who had a poor command of English and one who was unable to hold a pen due to arthritis were excluded from the study. Thirty-three women (group A) granted and 10 (group B) withheld consent for inclusion in the proposed study (Table 1).

Table 1. Anxiety scores from the state-trait anxiety inventory (STAI) and linear analogue scale (LA), age and type of surgery in patients who granted (group A) and withheld (group B) consent for inclusion in an hypothetical study of anxiolytic premedication.

STAI	LA (mm)	Age (years)	Operation
<i>Group A (n = 33)</i>			
20	10	45	Minor
22	0	54	Minor
23	100	61	Minor
24	4	39	Minor
25	0	26	Intermediate
27	9	49	Major
28	5	44	Major
29	16	57	Minor
29	37	70	Major
31	6	64	Major
31	52	59	Minor
31	9	58	Minor
33	28	39	Major
35	5	51	Minor
35	34	61	Major
36	24	48	Major
36	8	44	Minor
38	32	47	Major
38	38	38	Major
38	30	47	Major
42	47	40	Major
42	34	44	Major
43	28	56	Minor
44	45	31	Major
45	38	59	Minor
48	60	36	Minor
48	82	37	Minor
49	39	53	Minor
49	39	34	Intermediate
54	60	33	Minor
56	87	26	Major
62	47	56	Minor
73	99	35	Minor
<i>Group B (n = 10)</i>			
40	45	45	Major
48	69	44	Major
49	57	37	Intermediate
49	94	39	Major
50	59	32	Major
57	67	41	Major
59	60	29	Minor
59	78	46	Minor
59	99	46	Major
70	88	35	Major

The median age of group A, 47 years (range 26–70 years), was not significantly different from that in group B, 40 (29–46) years. The nature of the proposed surgery was classed as major (hysterectomy, ovarian cystectomy or tubal recanalisation), intermediate (laparoscopy or colporrhaphy) or minor (dilatation and curettage, cervical biopsy or cautery). Only three intermediate cases were included, two in group A and one in group B, and these were combined with the minor cases for analysis. There was no significant difference in the number who granted consent for

Table 2. Nature of proposed surgery related to the granting (group A) or withholding (group B) of consent for inclusion in a research project.

	Surgery		Totals
	Intermediate and minor	Major	
Group A	19	14	33
Group B	3	7	10
Totals	22	21	43

$\chi^2 = 2.34$, not significant.

inclusion in the proposed study (Table 2) when patients who had major surgery were compared with those with minor or intermediate surgery.

The median STAI score of group A, 36 (range 20–73), was significantly ($p < 0.01$) lower than that of group B, 53.5 (40–70). The median linear analogue score of group A, 34 mm (range 0–100 mm), was also significantly ($p < 0.01$) lower than that of group B, 68 (45–99) mm (Fig. 1). There was good agreement between the two methods of anxiety assessment ($r = 0.73$, $p < 0.01$).

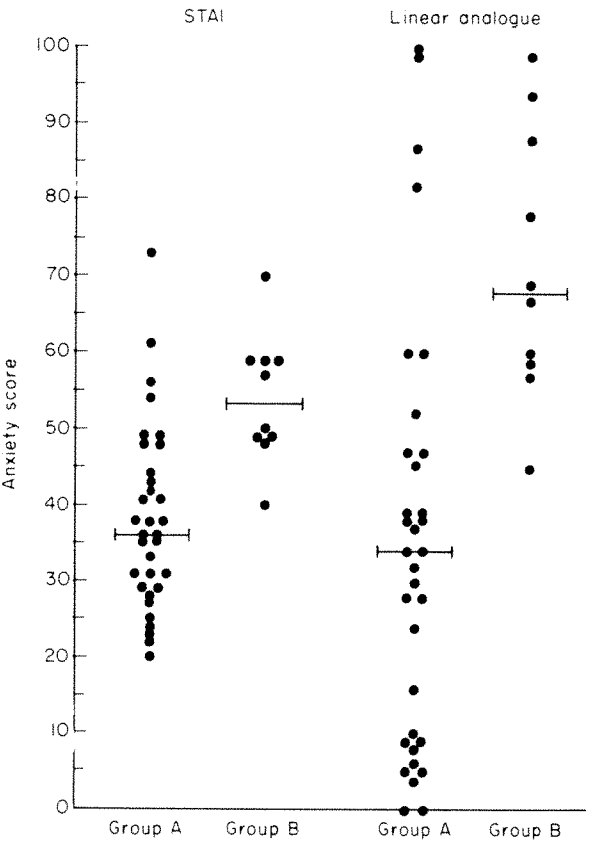


Fig. 1. Anxiety scores measured by the state-trait anxiety inventory (STAI) and a 10-cm linear analogue scale for subjects who granted (group A) and withheld (group B) consent for inclusion in a study of anxiolytic pre-anaesthetic medication (median for each group indicated).

Discussion

The decision to grant or withhold consent for participation in a clinical trial involves many factors. The interview in this study was standardised and rehearsed in an attempt to achieve uniformity. Two further factors which may influence the decision, namely age and the nature of proposed

surgery, were compared between the two groups. A significant difference was seen in anxiety assessed by both the STAI and the linear analogue scale between women who granted and those who withheld consent for inclusion in the proposed study. It is suggested that high anxiety levels predispose to the withholding of consent and that request of informed consent may lead anxious subjects to exclude themselves from study. A response to anxiolytic therapy is not seen unless the subject is anxious, and the response increases as anxiety levels rise; the exclusion of subjects with the highest anxiety will therefore reduce the response of a group to anxiolytic treatment. A reduction in sensitivity of the study will result from the bias in sampling.

Normative data for the STAI give basal values for anxiety levels. Fig. 2 shows STAI scores for the women

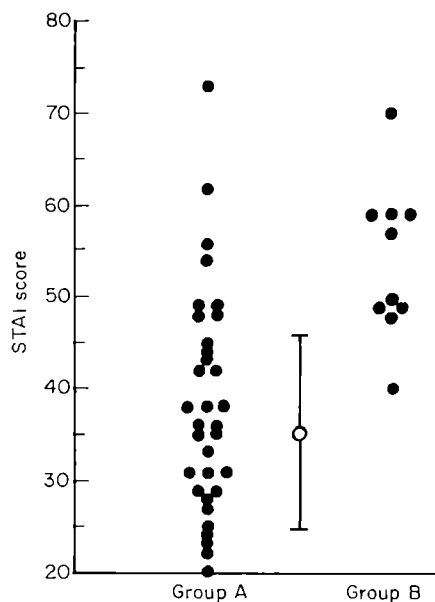


Fig. 2. Anxiety scores measured by the state-trait anxiety inventory (STAI) for subjects who granted (group A) and withheld (group B) consent for inclusion in a study of anxiolytic pre-anaesthetic medication. Also shown is the mean (SD) STAI score for working American women (\bar{x}).

in this study and for working American women (mean 35.2, SD 10.61). Few of the subjects in group A had raised anxiety levels and it might have been difficult to demonstrate an anxiolytic effect even had one existed, if the proposed trial had been performed on these women. The sensitivity of the method could be increased by application of a threshold anxiety level below which subjects would not be entered into the trial. However, Fig. 2 shows that as the threshold is raised, so fewer subjects are eligible for entry and a greater proportion of these withhold consent for inclusion. It would be difficult in this situation to recruit sufficient numbers, and it is doubtful whether such a trial would be valid with a significant proportion of eligible subjects excluding themselves.

How then are highly anxious subjects to be included in a study; is it ethical to proceed without consent? The Nuremberg Code³ indicates not: 'The voluntary consent of the human subject is absolutely essential'. However, the Declaration of Helsinki⁴ applies the basic principle that each potential subject must be 'adequately informed' and recognises in the case of clinical research, that the doctor must be free to use a new therapeutic measure if in his or her judgment it offers hope of alleviation of suffering. There seems little ground for ethical objection in a comparison of two established premedications, especially if both agents are in regular clinical use within the hospital concerned. The testing of a novel compound without consent might be ethical if good evidence were available to suggest that its use as premedication would be at least as effective as established agents; such evidence might relate to its anxiolytic properties in other situations. Subjects known to have high levels of anxiety would be denied active therapy if a placebo were used. However, it could be argued that the placebo effect is significant in the relief of anxiety and to inform the patient that placebo was in use would deprive him of such relief.

The use of a wide selection of sedative and anxiolytic agents for pre-anaesthetic medication suggests that none is entirely satisfactory. It is likely that novel agents will be produced with claims of greater efficacy, and that objective evaluation will be needed. It is concluded from this study that patients with high levels of pre-operative anxiety who are most in need of anxiolysis, are more likely to withhold consent for inclusion in studies of premedication than are those with less anxiety. It may be necessary in order to establish efficacy in these patients, to proceed without obtaining their consent. Whether or not it is justified to do so, must be judged by an independent ethical committee on the basis of specific proposals.

Acknowledgments

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References

1. SPIELBERGER CD, GORSUCH RL, LUSHENE R, VAGG PR, JACOBS GA. *Manual for the State-Trait Anxiety Inventory, STAI (Form Y)*. Palo Alto, CA: Consulting Psychologists' Press, 1983.
2. AITKEN RCB. Measurement of feelings using visual analogue scales. *Proceedings of the Royal Society of Medicine* 1969; **62**: 989-93.
3. *The Nuremberg Code* (1947). In: DUNCAN AS, DUNSTAN GR, WELBOURN RB, eds. *Dictionary of medical ethics*. London: Darton, Longman & Todd, 1981: 130-2.
4. *Declaration of Helsinki* (1964, revised 1975). In: DUNCAN AS, DUNSTAN GR, WELBOURN RB, eds. *Dictionary of medical ethics*. London: Darton, Longman & Todd, 1981: 132-5.

Intranasal sufentanil for pre-operative sedation

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Summary

Sufentanil, a short-acting and potent narcotic agent, was studied as a premedicant administered by the nasal route. A total dose of 5 µg appeared to be too low, while either 10 or 20 µg was very effective in producing sedation. Side effects were minor. There appeared to be no differences between nose drops and spray. In a further study, sufentanil nose drops were compared with saline 0.9% in a double-blind fashion. Sedation of rapid onset but of limited duration was observed in the majority of patients who received sufentanil.

Key words

*Analgesics; sufentanil.
Premedication.*

Pre-operative medication is often given reluctantly, since the commonly used regimens are long-acting, delay awakening or produce discomfort because of intramuscular administration. There is a growing interest as a result, in shorter-acting compounds and alternative routes of administration. Intranasal drug delivery, the administration of a compound through the nasal mucosa, may offer some advantages, since the blood supply of the nasal cavity bypasses the liver and enters the systemic circulation directly. This makes nasal administration superior to the oral route for drugs which are unstable in the gastrointestinal tract or which are metabolised substantially in the liver.

Sufentanil, a short-acting narcotic agent, might be suitable for intranasal administration, since it has a high potency/volume ratio. Even low doses (0.15 µg/kg) administered intramuscularly induce sedation in 50% of patients with chronic pain.¹ Somnolence following epidural administration of 50 µg sufentanil has been reported.² The aim of this study was to investigate whether low dose intranasal sufentanil produces pre-operative sedation without the induction of typical adverse reactions (nausea, vomiting, dysphoria, etc.) to opioids.

Patients and methods

Study 1

Forty healthy adult patients, free from colds or nasopharyngeal problems and who were scheduled for a variety

of minor surgical procedures, were included in an open dose-finding study. Informed consent was obtained. No other sedatives or narcotics were given during the 8 hours before surgery. Nasal sufentanil was administered at least one hour before induction of anaesthesia, using a 50 µg/ml solution either as a nose spray (1 puff = 0.1 ml, or 5 µg) or as nose drops (1 drop = 2.5 µg). Each patient was allocated to one of four groups and received 1, 2 or 4 puffs, or 4 drops, of sufentanil.

A standard nasal spray device was filled with 5 ml solution and primed by activating the pump a few times. The applicator tip was introduced 0.5 cm into each nostril, with the patient in an upright position. The nasal drops were administered with the patient supine. The head was tilted back and the solution dispensed equally between both nostrils during normal breathing. The head was then turned to the right and the left, and then back to the original position.

Study 2

In a second (double-blind) study, 40 patients of ASA grade 1 or 2 were assigned randomly to one of two groups and received nose drops of either sufentanil or saline 0.9% in a dose of 1 drop per 10 kg body weight, never exceeding a maximum dose of 8 drops. Measurements and observations before administration and after 5, 10, 20, 40 and 60 minutes, were made in a room close to the operating theatre.

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All administrations and observations were undertaken by the same physician.

Systolic arterial pressure, heart rate and respiratory rate were recorded simultaneously. The degree of sedation was graded as: 0 (absent), no sedation, patient fully awake; 1 (slight), heavy eyelids, patient felt sleepy; 2 (moderate), patient closed eyes when not stimulated but reacted to any noise; 3 (marked), eyes closed, not interested in the environment and eyes opened only when patient talked to; 4 (extreme), no reaction to verbal stimulation, eyes opened only on command, normal conversation not possible.

Other observations comprised anxiety (absent, moderate or severe), possible side effects of the drug, acceptance and subjective impressions of the patient.

No tests were included in the study to detect amnesic properties of sufentanil. Results were analysed statistically using the Mann-Whitney *U* test.

Results

Study 1

A dose of 5 µg sufentanil administered via a nose spray appeared to be insufficient, since only three patients in this group showed slight to moderate sedation (grade 1–2) of short duration (Table 1). Sedation was achieved in all but

one of the patients who received a dose of 10 µg. The onset of sedation was rapid (median 10 minutes) and in five patients the effect was still present at induction of anaesthesia 60 minutes later. Effective sedation (grade 2–3) was observed up to 50 (SD9) min after administration. Increasing the dose to 20 µg (4 sprays) did not improve the results, although side effects were not observed more frequently.

Results when sufentanil was administered as nose drops in a total dose of 10 µg were comparable with those obtained using the same dose as a spray (grade 2–3 observed in eight patients). Onset of sedation was noted at a median of 10 minutes (range 5–30 minutes), and the average duration was 40.8 (10–55) minutes.

Major changes in vital parameters were not observed in any of the 40 patients. The most frequent side effect was a short (10–15 minutes) period of dizziness aggravated by the erect posture; this occurred in less than 20% of the patients.

Study 2

Thirty-nine patients completed the study. One patient was excluded because a parenteral premedication was administered inadvertently. Both groups were comparable

Table 1. Results of dose-finding study

Dose	Median age, years (range)	Sedation *				Median onset, minutes (range)
		Absent	Slight	Moderate	Marked	
<i>Nasal spray</i>						
5 µg (n = 10)	30 (14–37)	7	2	1	0	12.5 (10–15)
10 µg (n = 10)	42 (16–70)	1	0	3	6	10 (5–20)
20 µg (n = 10)	32 (28–49)	1	1	4	4	10 (5–10)
<i>Nose drops</i>						
10 µg (n = 10)	53 (27–70)	1	1	5	3	10 (5–30)

* Number of patients.

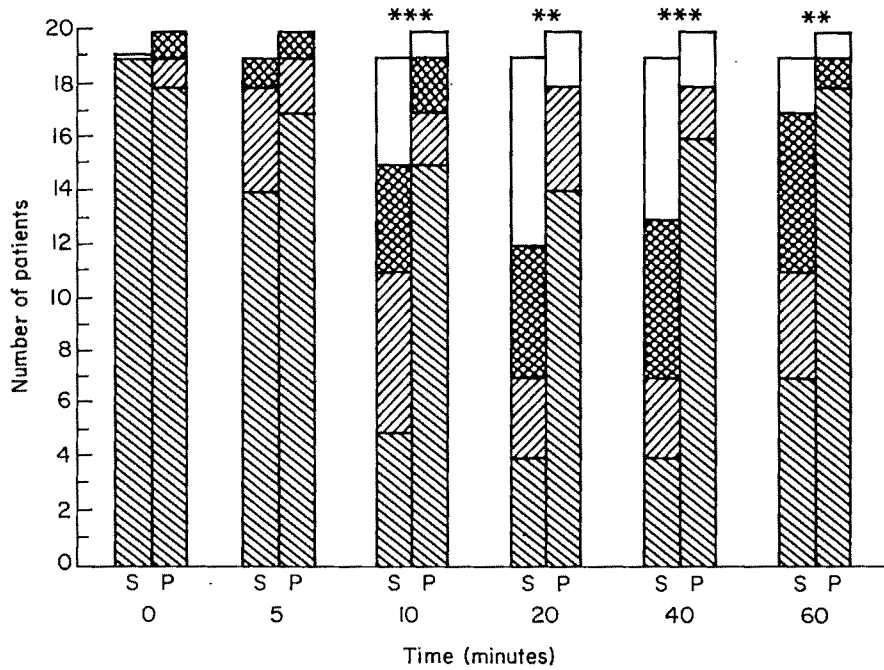


Fig. 1. Sedation scores in double-blind study. S, Sufentanil; P, saline 0.9%. Sedation graded as: □, absent; ▨, slight; ▩, moderate; ■, marked. ** p < 0.005; *** p < 0.001.

Table 2. Patient data for double-blind trial.

	Group A, sufentanil (n = 19)	Group B, placebo (n = 20)
Median age, years (range)	39 (19–62)	38 (17–75)
Median weight, kg (range)	65 (46–76)	63 (47–106)
Sex, F/M	17/2	13/7

in respect of age, weight and sex (Table 2). The results show that sufentanil produced a significantly greater degree of sedation. Eight patients in the sufentanil group showed moderate or marked (grade 2–3) sedation 10 minutes after administration, compared with three in the placebo group (Fig. 1). Twelve patients in the sufentanil group but only two in the placebo group showed a good response at 20 and 40 minutes, and eight patients in the sufentanil group were clearly sedated at 60 minutes.

Vital parameters remained stable throughout the observation period (Figs 2 and 3). Vertigo was reported by three patients (16%) who received sufentanil, and two patients, one in each group, required an antiemetic drug.

Four (21%) of the patients who received sufentanil graded their pre-operative fear as severe, and a decrease in anxiety was noted in all of these after administration of the drops. However, an anxiolytic effect was also registered in one of the two very anxious patients in the placebo group. A small decrease in the heart rate (by 4%, but in five sufentanil-treated patients by more than 15%) may also reflect some reduction of anxiety. The most common subjective impressions reported spontaneously in the sufentanil group were heaviness in the extremities (36%) and a sense of well-being.

Discussion

Differing views exist about the value of a standardised premedication in all patients who undergo surgery. The timing and the route of drug administration may be as important as the drug selected. Parenteral administration has become unpopular and several alternative routes have been investigated. Rectal administration of premedicant drugs has been used in paediatric practice but is not accepted well by all children; benzodiazepines have been used most commonly, but morphine, hyoscine and other mixtures are also advocated.³ Oral and sublingual routes of administration of benzodiazepines are effective,^{4,5} al-

though systemic resorption following oral administration may be delayed until 120 minutes after drug intake.⁶

We decided to study the nasal route of administration and selected sufentanil because of its high potency/volume ratio in comparison with commonly used benzodiazepines; large volumes of these agents would have been required, and ‘drowning’ of the nasal mucosa should be avoided. Information on the possible effective dose of sufentanil was not available and we decided to start with an open dose-finding study followed by a randomised, prospective double-blind study.

It was concluded from the dose-finding study, that 5 µg was insufficient, whereas the 10- and 20-µg doses provided sedation in the majority of patients. The highest dose was not more effective, although still safe, since side effects were not observed more frequently than in the 10-µg group.

The 10-µg dose administered as nose drops produced the same results and supports the study by Hardy *et al.*⁷ which demonstrated a better nasal spread of labelled albumin after a single drop than after single spray. Three drops appeared to cover the walls of the whole (unilateral) nasal cavity. For this reason, it was decided to use the nasal drops for the double-blind study. The dose selected was 1 drop per 10 kg body weight (maximum total dose 20 µg); this is equivalent to 3 drops in each nostril for a patient who weighs 60 kg, and provides optimal mucosal covering.

The results of this placebo-controlled study suggest that sufentanil given in a low dose by the nasal route produces effective pre-operative sedation in the majority of patients. The onset of sedation was very rapid, whereas drugs given

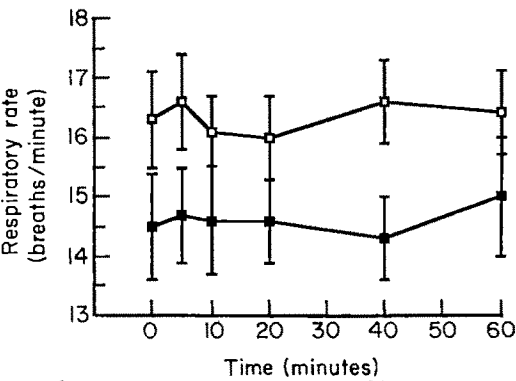


Fig. 3. Respiratory rate (mean, SEM) in double-blind study. ■, Sufentanil; □, placebo.

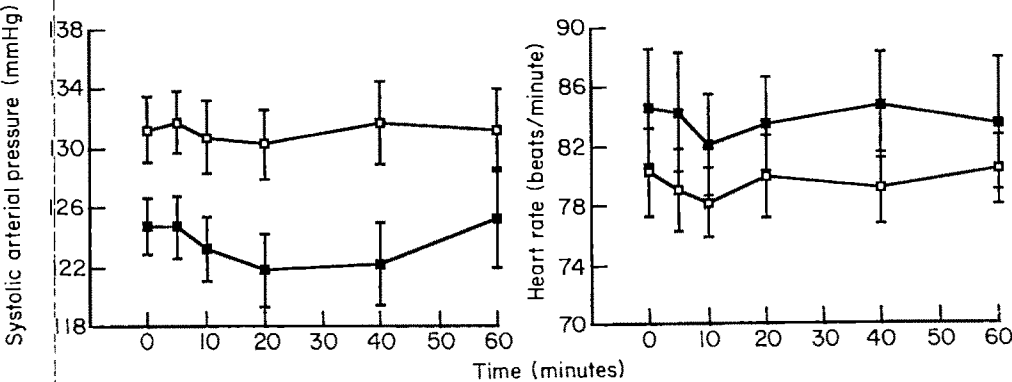


Fig. 2. Systolic arterial pressure and heart rate (mean, SEM) in double-blind study. ■, Sufentanil; □, placebo.

intramuscularly or orally may have a latency time of 30–60 minutes.⁸

The effect 60 minutes after application was clearly decreasing. This may be a disadvantage, although pharmacological interference with peri-operative drugs will be minimal. The initial dose might be repeated if the response to the first dose was insufficient or surgery delayed.

McKay and Dundee⁹ compared sedation scores after oral administration of diazepam 10 mg, flunitrazepam 1 mg or lorazepam 2 mg, and found marked drowsiness or sleep in 60–70% of patients. In the present study, 79% of patients were moderately or well sedated after sufentanil administration, although only 63% of patients exhibited these degrees of sedation at any one observation time, because of the short duration of action and the occasionally late onset.

Nasal sufentanil appeared to be relatively free of the usual opioid side effects. A short period of dizziness was the main side effect, although even benzodiazepines are not free from this symptom.⁵ Acceptance of this method of premedication was very high, possibly because of the absence of discomfort caused by injection. The rapid onset may allow optimal timing, especially in semi-urgent procedures. Only adult patients were studied but this form of premedication might also have some advantages for paediatric use. Future work should include a more sensitive study of the

effects on anxiety, respiratory function and the correlation of clinical effects with plasma concentrations.

References

1. CATHELIN M, VIGNES R, MALKI A, VIARS P. Sufentanil and morphine by intramuscular injection. Side effects compared in conscious man. *Anesthésie, Analgésie, Réanimation* 1981; **38**: 27–32.
2. DONADONI R, ROLLY G, NOORDUIN H, VANDEN BUSSCHE G. Peridural sufentanil for postoperative pain relief. *Anaesthesia* 1985; **40**: 634–8.
3. LINDAHL S, OLSSON AK, THOMSON D. Rectal premedication in childhood. Use of diazepam, morphine and hyoscine. *Anaesthesia* 1981; **36**: 376–9.
4. KANTO J. Benzodiazepines as oral premedicants. *British Journal of Anaesthesia* 1981; **53**: 1179–87.
5. GALE GD, GALLOON S, PORTER WR. Sublingual lorazepam: a better premedication? *British Journal of Anaesthesia* 1983; **55**: 761–5.
6. RICHARDS DG, MCPHERSON JJ, EVANS KT, ROSEN M. Effect of volume of water taken with diazepam tablets on absorption. *British Journal of Anaesthesia* 1986; **58**: 41–4.
7. HARDY JG, LEE SW, WILSON CG. Intranasal drug delivery by spray and drops. *Journal of Pharmaceutics and Pharmacology* 1985; **37**: 294–7.
8. WHITE PF. Pharmacologic and clinical aspects of preoperative medication. *Anesthesia and Analgesia* 1986; **65**: 963–74.
9. MCKAY AC, DUNDEE JW. Effect of oral benzodiazepines on memory. *British Journal of Anaesthesia* 1980; **52**: 1247–57.

Benzodiazepine intoxication treated with flumazenil (Anexate, RO 15-1788)

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Summary

The efficacy and safety of flumazenil were assessed in comparison to placebo in a double-blind randomised study of 31 adults intoxicated with benzodiazepines. The criteria of efficacy were the degree of sedation, and orientation in time and space. Patients who received flumazenil awoke within minutes but central depression returned partly one hour later, which reflects the short elimination half-life of the drug. Side effects were few and the results indicate that flumazenil is effective in the primary management of benzodiazepine overdose and in states where benzodiazepines have been taken with other drugs.

Key words

Hypnotics; benzodiazepines.

Antagonists; benzodiazepine; flumazenil.

Benzodiazepines are involved increasingly in suicidal or accidental overdose, mostly in combination with ethanol or other drugs. Benzodiazepines alone are rarely fatal even in high doses but they potentiate the central depressant effects of many other agents.¹⁻⁵ A benzodiazepine antagonist might be useful in the treatment of overdose through reduction in the comatose state and in the lengths of stay in the intensive care unit. Such an antagonist might also eliminate the potentiating effects of benzodiazepines and be a simple diagnostic tool in the detection of a benzodiazepine in some neurological and psychiatric disorders where the exact diagnosis is unclear.⁶⁻⁸

Flumazenil (Anexate, RO 15-1788) is an imidazo-benzodiazepine which blocks the central effects of the benzodiazepines. The antagonist has a high affinity for the benzodiazepine receptors in the brain and acts as a strong competitive inhibitor. It does not interfere with the metabolism of diazepam.⁹

The purpose of this study was to evaluate the efficacy of flumazenil in reversing the central effects of benzodiazepines taken in overdose and to evaluate its local and general safety.

Methods

Thirty-two consecutive patients aged 18-70 years who were thought to have taken a benzodiazepine in overdose were studied in a double-blind randomised fashion. The investigation was carried out in accordance with the Helsinki

11 declaration and was approved by the local ethical committee.

The degree of sedation on admission to hospital was evaluated on a modified Glasgow coma scale¹⁰ (Table 1).

Table 1. Modified Glasgow coma scale.

Eye opening
1, none
2, to pain (stimulus in the limbs)
3, to speech
4, spontaneous
Best motor response (of the limbs)
1, none
2, extension
3, flexion
4, withdrawal
5, localisation
6, to command
Best verbal response
1, none
2, incomprehensible
3, inappropriate
4, confused
5, orientated

Patients who scored 14 or 15 points on this scale, who were known to suffer from liver or kidney disease or who were pregnant, were excluded from the study. The stomach was aspirated and activated carbon administered to all patients.

Blood and urine samples were taken for analysis of

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ethanol, barbiturates, benzodiazepines, salicylic acid, opioids, dextropropoxyphene paracetamol and methaqualone. The benzodiazepine concentration was measured using a radioreceptor assay method¹¹ and expressed as the equivalent concentration of lorazepam (mmol/litre).

Patients were allocated randomly to two groups. A bolus of flumazenil or placebo 0.3 mg (3 ml) was given through a separate cannula in a vein on the dorsum of the right hand. Another 0.3 mg was injected after 60 seconds if the patient did not wake up, and then 0.2 mg every 60 seconds to a maximum of 1.0 mg.

Arterial blood pressure, heart rate, respiratory rate, degree of sedation and orientation in time and space were recorded before injection and at 5, 15, 30, 60, 180, 300 minutes and 24 hours. Orientation in time and space was assessed as follows: 1, no response; 2, total disorientation; 3, orientation only in space; 4, orientation only in time; 5, orientation both in time and space. Local and central side effects were recorded.

Results are given as median and range. Comparability between groups was assessed by the Mann-Whitney and Fisher's exact test. Arterial blood pressure, heart rate, respiratory rate, degree of sedation and orientation in time and space were analysed by a combination of the Mann-Whitney and Friedman tests which corresponds to non-parametric analysis of variance for a two-factor design. The level of significance was chosen as 5%.

Results

There were 16 patients in each group, 13 male and 19 female, with a median age of 37 years (range 23-67 years). One patient from the placebo group was excluded because benzodiazepines were not detectable in the blood. The groups were comparable with regard to sex, age, weight, height, concentration of benzodiazepines, ethanol and other drugs in the blood (Table 2), and the number of patients with drugs in their urine (Table 3). Ethanol was found in

Table 2. Concentration of drugs in blood expressed as median (range).

Group	Benzodia- zepines, µg/litre	Ethanol, g/litre	Barbitu- rates, µmol/litre	Salicylic acid, mmol/litre
Flumazenil	188 (39-945)	1.99 (0-2.94)	33 (n = 3)	0.23 (n = 2)
Placebo	200 (67-1340)	0.23 (0-2.62)	37 (n = 3)	0 (n = 0)
Significance	NS	NS	NS	NS

NS, Not significant.

Table 3. Numbers of patients with drugs in urine.

Group	Opioids	Dextro- propoxi- phene	Para- cetamol	Metha- qualone	Benzodia- zepines
Flumazenil	0	1	4	2	13
Placebo	2	4	1	0	14
Significance	NS	NS	NS	NS	NS

NS, Not significant.

the blood of 24 patients and 13 patients had taken more than one drug.

Patients in the control group all received 1 mg (10 ml) of placebo. Those in the treatment group received a mean of

0.96 mg (9.6 ml) (range 0.3-1 mg) of flumazenil. Patients in the flumazenil group awoke significantly faster as judged by the modified Glasgow coma scale and by orientation in time and space (Tables 4 and 5). There were no significant

Table 4. Coma scale results expressed as median score (first-third quartiles).

Time	Flumazenil	Control
Before injection	6.3 (5-7)	6.0 (4-7)
5 minutes	14.6 (13-15)	7.0 (6-8)
15 minutes	14.6 (13-15)	7.8 (6-9)
30 minutes	14.0 (11-15)	7.8 (6-10)
60 minutes	11.2 (9-14)	9.8 (7-11)
180 minutes	12.0 (9-14)	10.8 (9-12)
300 minutes	12.3 (9-14)	12.8 (10-14)

Table 5. Orientation in time and space expressed as median score (first-third quartiles).

Time	Flumazenil	Control
Before injection	1.0 (1-1)	1.1 (1-1)
5 minutes	3.5 (2-4)	1.1 (1-1)
15 minutes	4.5 (2-5)	1.2 (1-1)
30 minutes	4.0 (2-5)	1.2 (1-1)
60 minutes	2.0 (1-5)	1.4 (1-2)
180 minutes	2.3 (1-5)	1.9 (1-2)
300 minutes	3.2 (1-5)	2.3 (2-5)

differences between the groups after one hour, partly because patients in the control group awoke spontaneously and partly because the effect of the antagonist decreased.

There was no significant difference in arterial pressure or respiratory rate between the two groups. There was a significantly higher heart rate in the flumazenil group but this was not clinically important.

One patient in each group showed slight redness at the injection site. Six patients in the flumazenil group were restless and two were nauseated. Four patients were restless in the placebo group. There were no significant differences with regard to side effects.

Discussion

Several attempts have been made to find an antagonist to the benzodiazepines. Naloxone has been proposed¹² but its clinical usefulness could not be demonstrated.¹³ Cholinesterase inhibitors have been claimed to reverse the sedative effects of benzodiazepines¹⁴ but this has not been confirmed.¹⁵ Aminophylline has been shown to reverse diazepam sedation,¹⁶⁻¹⁸ perhaps because it is a general adenosine antagonist; one of the suggested mechanisms of diazepam sedation is potentiation of the depressant effects of adenosine.^{18,19}

The practical implications of a specific benzodiazepine antagonist that blocks the pharmacological effects of benzodiazepines at the central receptor level have been discussed.²⁰ Jensen *et al.*²¹ found fast awakening, return of orientation in time and space, elimination of amnesia, and a higher *PO*₂ and lower *PCO*₂ level in arterial blood in patients who received flumazenil after general anaesthesia with flunitrazepam, fentanyl and pancuronium and nitrous oxide-oxygen. Wolf *et al.*²² found awakening within seconds or a few minutes in 100 women who underwent abortion induced under midazolam anaesthesia with flumazenil.



effectively reverses sedation and amnesia due to diazepam in outpatients who undergo gastroscopy.²³

The results of the present study establish that this new antagonist effectively reverses the central effects associated with benzodiazepine overdose. All patients who received flumazenil were fully awake and orientated within 5 minutes whereas previously they reacted only to painful stimuli by flexing the limbs. There was an increase in the level of sedation and a decrease in orientation after one hour but only to a state where the patients were confused; they reacted to pain by withdrawal of the limbs and opened their eyes when spoken to. The partial return of central depression reflects the short elimination half-life (approximately 50 minutes) of flumazenil. The possibility of repeating the procedure at 45 minutes could be considered, after which central nervous system depression should not return.

Ethanol was found in the blood in the majority of the patients and many were intoxicated with several different drugs. The benzodiazepine component in these cases was promptly unmasked by flumazenil. This is a very useful diagnostic quality in patients with overdose of sedative drugs which cannot be identified quickly by clinical history.

References

1. GREENBLATT DJ, ALLEN MD, NOEL BJ, SHADER RI. Acute overdosage with benzodiazepine derivatives. *Clinical Pharmacology and Therapeutics* 1977; **21**: 497-514.
2. BJELDAGER PAL, BREUM L, MUNCK LK, NORDESTGAARD AG, HUNDING A. Benzodiazepine poisoning in a poisoning treatment centre in 1980. *Ugeskrift for Læger* 1984; **146**: 503-7.
3. JACOBSEN JB, NIELSEN H, RINGSTED C, ANDERSEN PK. Deliberate self-poisoning. 5-year case material from an intensive care unit. *Ugeskrift for Læger* 1981; **143**: 2430-3.
4. PROUDFOOT AT, PARK J. Changing pattern of drugs used for self-poisoning. *British Medical Journal* 1978; **1**: 90-3.
5. PRESCOTT LF. Safety of the benzodiazepines. In: COSTA E, ed. *The benzodiazepines*. New York: Raven Press, 1983.
6. HAEPFELY W, BONETTI EP, BURKHARD WP, CUMIN R et al. Benzodiazepine antagonists. In: COSTA E, ed. *The benzodiazepines*. New York: Raven Press, 1983.
7. HOFER P, SCOLLO-LAVIZZARI G. Benzodiazepine antagonist RO 15-1788 in self-poisoning. *Archives of International Medicine* 1985; **145**: 663-4.
8. SCOLLO-LAVIZZARI G. First clinical investigation of the benzodiazepine antagonist RO 15-1788 in comatose patients. *European Neurology* 1983; **22**: 7-11.
9. DARRAGH A, LAMBE R, KENNY M, BRICK I, TAAFFE W. RO 15-1788 antagonises the central effects of diazepam in man without altering diazepam bioavailability. *British Journal of Clinical Pharmacology* 1982; **14**: 677-82.
10. TEASDALE G, JENNETT B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974; **2**: 81-4.
11. LUND J. Radioreceptor assay for benzodiazepines in biological fluids using a new dry and stable receptor preparation. *Scandinavian Journal of Clinical and Laboratory Investigation* 1981; **41**: 275-80.
12. BELL BF. The use of naloxone in the treatment of diazepam poisoning. *Journal of Pediatrics* 1975; **87**: 803-4.
13. HUTTEL MS, CHRISTENSEN KN. Naloxone as antidote in benzodiazepine poisoning. *Ugeskrift for Læger* 1979; **141**: 1979-81.
14. PEDERSEN JE. Physostigmine: an antidote in diazepam poisoning. *Ugeskrift for Læger* 1985; **147**: 3586-7.
15. GARBER JG, OMSKY AJ, ORKIN FK, QUINN P. Physostigmine-atropine solution fails to reverse diazepam sedation. *Anesthesia and Analgesia* 1980; **59**: 58-60.
16. ARVIDSSON S, NIEMAND D, MARTINELL S, EKSTROM-JODAL B. Aminophylline reversal of diazepam sedation. *Anaesthesia* 1984; **39**: 806-9.
17. STIRT JA. Aminophylline is a diazepam antagonist. *Anesthesia and Analgesia* 1981; **60**: 767-8.
18. NIEMAND D, MARTINELL DS, ARVIDSSON S, EKSTROM-JODAL B, SVEDMYR N. Adenosine in the inhibition of diazepam sedation by aminophylline. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 493-5.
19. ARVIDSSON SB, EKSTROM-JODAL B, MARTINELL SAG, NIEMAND D. Aminophylline antagonises diazepam sedation. *Lancet* 1982; **2**: 1467.
20. ASHTON CH. Benzodiazepine overdose: are specific antagonists useful? *British Medical Journal* 1985; **290**: 805-6.
21. JENSEN S, KIRKEGAARD L, ANDERSON BN. Randomized clinical investigation of RO 15-1788, a benzodiazepine antagonist, in reversing the central effects of flunitrazepam. *European Journal of Anaesthesiology* 1987; **4**: 113-8.
22. WOLFF J, CARL P, CLAUSEN TG, MIKKELSEN BO. RO 15-1788 for postoperative recovery. A randomised clinical trial in patients undergoing minor surgical procedures under midazolam anaesthesia. *Anaesthesia* 1986; **41**: 1001-6.
23. KIRKEGAARD L, KNUDSEN L, JENSEN S, KRUSE A. Benzodiazepine antagonist RO 15-1788. Antagonism of diazepam sedation in outpatients undergoing gastroscopy. *Anaesthesia* 1986; **41**: 1184-8.

A comparison of rectal diclofenac with intramuscular papaveretum or placebo for pain relief following tonsillectomy

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Summary

A controlled investigation was conducted to compare the effectiveness of diclofenac and papaveretum in the prevention of pain and restlessness after tonsillectomy in children. Sixty children between 3 and 13 years of age were randomly allocated to receive rectal diclofenac 2 mg/kg, intramuscular papaveretum 0.2 mg/kg or no medication immediately after induction of anaesthesia. Pain and appearance were assessed 1, 3 and 6 hours postoperatively, and the following morning. The assessments were double-blind and performed by the same observer. No significant differences in postoperative pain were found between the groups at any time. The use of diclofenac was associated with a significantly more rapid return to calm wakefulness and had significantly less effect upon respiratory rate. Consumption of paracetamol on the day of operation was significantly less in the diclofenac group. Diclofenac may offer advantages compared to papaveretum with regard to safety and convenience for use in the treatment of pain after tonsillectomy in children.

Key words

Analgesics; papaveretum, diclofenac.

Pain; postoperative.

The provision of adequate analgesia is necessary after any painful operation and in the case of tonsillectomy, it is desirable to ensure smooth awakening since increased vascular congestion of the head and neck associated with crying may precipitate bleeding.¹ Children are often afraid of injections and the use of an opioid given intra-operatively may avoid the necessity for intramuscular administration in the immediate postoperative period. However, opioid administration, particularly to small children, carries the potential disadvantage of respiratory depression which may be compounded by postoperative problems following surgery to the pharynx. For this reason many anaesthetists prefer to withhold opioids until the return of respiratory reflexes postoperatively.

Non-steroidal anti-inflammatory analgesic drugs (NSAID) have been employed previously with success as postoperative analgesics.² They may prove particularly useful in conditions where a degree of tissue inflammation contributes to pain. Rectally administered indomethacin was proved to be effective as a postoperative analgesic in association with the concurrent use of intramuscular morphine,³ and diclofenac has been employed as a postoperative analgesic either alone or in combination with opioids. Dommerby and Rasmussen⁴ showed in patients

aged 12 years and over who underwent tonsillectomy, that rectal diclofenac given immediately postoperatively and continued thereafter produced satisfactory analgesia in comparison with placebo. The present study was therefore undertaken to evaluate the efficacy of rectal diclofenac and compare it with intramuscular papaveretum in children after tonsillectomy or adenotonsillectomy.

Methods

The investigation was approved by the district ethical committee. Sixty children admitted for tonsillectomy with or without adenoidectomy were studied. Written, informed parental consent was obtained for participation in the study; patients with a history of asthma, drug allergy, gastric erosion or sensitivity to opioids were not studied. They were allocated randomly to one of three treatment groups to receive intra-operatively either rectal diclofenac 2 mg/kg (group A), intramuscular papaveretum 0.2 mg/kg (group B) or no analgesia (control, group C).

Oral premedication with trimeprazine 2 mg/kg was given 90 minutes pre-operatively. Anaesthesia was induced by either intravenous thiopentone or by an inhalational technique using nitrous oxide, oxygen and halothane. The

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tracheas of all patients were intubated using a Rae-Mallinckrodt tube, facilitated by the use of suxamethonium if required. Each patient after induction of anaesthesia received either intramuscular papaveretum, rectal diclofenac or no medication according to the treatment group to which he/she was assigned. Anaesthesia was maintained with 67% nitrous oxide in oxygen supplemented with halothane, and all patients breathed spontaneously. A Jackson-Rees modification of Ayre's T-piece was used in children under 25 kg, and a Bain coaxial system in others. Anaesthesia was conducted by consultant members of the anaesthetic department.

The inhalational agents were withdrawn on completion of surgery, the patients awakened, their tracheas extubated and they were conveyed to the recovery area and thence to the ward. The children received postoperative analgesia of either intramuscular papaveretum 0.2 mg/kg or oral paracetamol 125–500 mg at the discretion of the nursing staff, if considered appropriate at this stage.

The investigator, who was blind to the group allocation of the patients and to any postoperative analgesia administered, assessed the patients postoperatively with reference to pain, appearance, side effects and respiratory rate. Pain was assessed as none/insignificant, or pain present. Appearance was graded on a four-point scale: asleep and calm; sleepy and restless; awake and calm; awake and restless. The presence or absence of any side effects including nausea and vomiting was noted. Respiratory rate was recorded for one minute. Assessments were undertaken on four occasions: 1, 3 and 6 hours postoperatively, and on the following morning. These times were chosen to coincide with the presumed peak analgesic effect of intra-operatively administered analgesia, the time of offset of such analgesia and approximately 18–24 hours postoperatively.⁵ The time and dosage of postoperative analgesic received were also recorded for each patient after the end of the investigation period.

Statistical analysis of the data for pain, appearance and the use of postoperative analgesia was performed using the Chi-squared test with Yates' correction. Between-group comparisons of parametric data were made using Student's unpaired *t*-test.

Results

A total of 60 children were studied, 20 patients in each treatment group. Demographic data are shown in Table 1.

Table 1. Patient demographic data, expressed as mean (SD).

Group	n	M:F	Age, years	Weight, kg
A (diclofenac 2 mg/kg)	20	6:14	7.6 (2.2)	28.2 (9.2)
B (papaveretum 0.2 mg/kg)	20	6:14	8.2* (3.5)	30.3* (9.6)
C (control, no analgesia)	20	10:10	6.9 (2.2)	24.0 (6.2)

* $p < 0.05$ compared with group C.

The mean age and weight of patients in group B were significantly different from those of group C ($p < 0.05$). The distribution of morning or afternoon surgery was equal between groups.

Five patients in group C were observed to have pain one hour postoperatively, but only two and one in groups A and B, respectively (Fig. 1). These numbers increased at 3 and 6 hours postoperatively but at no time was there any significant difference in the incidence of pain between treatment groups. Similar numbers in each treatment group had pain present the following morning.

Table 2 shows the observer assessments of patient appearance. Ninety-five percent of children in each group were asleep or sleepy one hour postoperatively. There were significantly ($p < 0.05$) more patients awake and calm at 3 and 6 hours postoperatively in group A compared to the two other treatment groups. No inter-group differences were apparent the following morning.

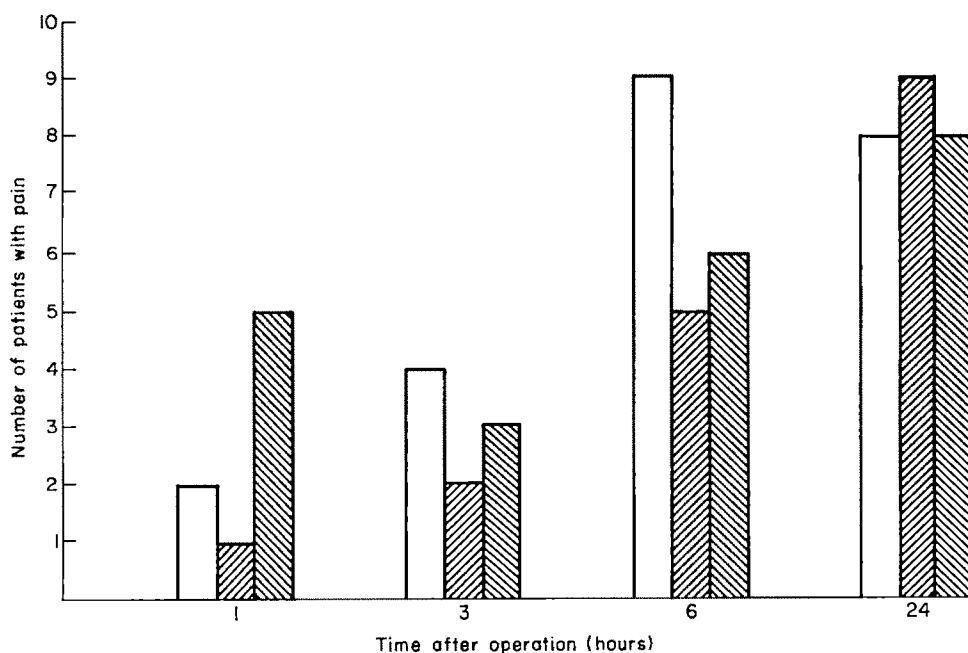


Fig. 1. Histogram of number of patients with pain 1, 3, 6 and 24 hours postoperatively. □, Group A (diclofenac 2 mg/kg); ▨, group B (papaveretum 0.2 mg/kg); ▩, group C (control, no analgesia).

Table 2. Comparison of grading of appearance postoperatively, expressed as numbers of patients.

Time (hours)	Group	Observer assessment of appearance			
		Asleep and calm	Sleepy and restless	Awake and calm	Awake and restless
1	A	18	1	0	1
	B	19	0	0	1
	C	15	4	0	1
3	A	11	1	8*	0
	B	18	2	0	0
	C	17	1	0	2
6	A	5	2	11*	2
	B	11	5	2	2
	C	9	5	2	4
24	A	0	0	20	0
	B	0	0	20	0
	C	0	0	20	0

* $p < 0.05$ compared to groups B and C.

There was no inter-group difference in respect of side effects of nausea or vomiting. One patient in group B vomited at 1 hour. No patient vomited at 3 hours but one child in each group vomited at 6 hours. One patient in group A vomited the following morning. No patient complained of nausea or appeared to be nauseated.

The mean respiratory rates of patients in groups B and C were significantly lower ($p < 0.01$) at 1 and 3 hours postoperatively than that of group A (Table 3). There were no

Table 3. Respiratory rate.

Time (hours)	Group	Mean	(SD)	Range
1	A	17.3*	(2.2)	14–24
	B	13.5	(2.2)	8–18
	C	14.2	(1.8)	12–18
3	A	17.6*	(2.6)	14–22
	B	14.7	(2.2)	10–18
	C	15.5	(1.8)	14–20
6	A	17.8	(1.8)	14–22
	B	16.7	(1.8)	14–22
	C	16.6	(1.8)	14–20
24	A	17.6	(1.8)	14–20
	B	17.7	(1.8)	16–20
	C	18.1	(1.8)	16–20

* $p < 0.01$ compared to groups B and C.

significant differences between groups in the respiratory rates 6 hours postoperatively and the following morning.

No patient in the groups that received intra-operative analgesia required postoperative papaveretum. The 20 children in the group that received no analgesia were given intramuscular papaveretum by the nursing staff at a mean time of 10 minutes (SEM 1.79) after their return to the ward (Table 4). This was administered because the nursing staff considered these children to have marked pain.

Ten patients in group A required paracetamol, and a mean dose of 350 mg (SEM 40.8) was given at a mean time of 7.3 hours (SEM 0.37) postoperatively. This number of patients was significantly ($p < 0.05$) less than in both other groups (Table 4). Patients in group B received a mean dose of 305 mg (SEM 30.7) paracetamol, 6.9 hours (SEM 0.24) postoperatively and in group C, a mean dose of 278.4 mg

Table 4. Postoperative analgesic requirements on day of operation, expressed as numbers of patients.

Group	Papaveretum 0.2 mg/kg	First dose of paracetamol	Second dose of paracetamol
A	0	10*	0
B	0	17	1
C	20†	17	4

* $p < 0.05$ compared to groups B and C.† $p < 0.01$ compared to groups A and B.

(SEM 67.8) was given 7.8 hours (SEM 0.3) postoperatively. One patient in group C and four patients in group B required a further dose of paracetamol on the day of operation. The postoperative recovery of all patients was uneventful and no other side effects were reported.

Discussion

This investigation indicates that tonsillectomy in children is a painful operation and requires some form of analgesia in the initial recovery period. Patients in the control group, who received no intra-operative analgesia, were given papaveretum by the nursing staff shortly after their return to the ward. Postoperative pain may have adverse psychological effects in the child.⁶ To awaken in pain can result in a restless and uncooperative patient, and it therefore seems preferable to prevent the onset of pain rather than to relieve its existence. This approach is supported by recent work that compared nalbuphine and morphine for the treatment of post-tonsillectomy pain;⁷ children were found to be more comfortable in recovery if they received analgesia at the end of surgery compared to those who received no analgesia. It was considered ethical to include a control group in the present investigation, since it is established practice with some anaesthetists to administer no intra-operative analgesia.

Our results indicate that intra-operative diclofenac offers satisfactory postoperative analgesia as compared with papaveretum, together with some specific advantages. There were no significant differences in analgesic efficacy assessed by the presence of pain. The measurement of pain in young children presents particular difficulties. The linear analogue scale is a useful research tool when scored by the subject.⁵ However, most children in this study were too young to grade their pain. We therefore used a simple observer grading of none/insignificant pain, or pain present. A child who was awake and calm yet acknowledged the presence of sore throat was graded to have pain present; this explains the slightly higher incidence of pain in the diclofenac group at 3 and 6 hours, when significantly more patients in this group were awake. Significantly less postoperative analgesia was required by patients who received diclofenac compared to those given either intra-operative or postoperative papaveretum. This is perhaps due to the anti-inflammatory action of diclofenac which may exert an effect upon the postoperative tissue reaction to surgery and result in a lesser degree of perceived pain.

Significant differences were found in the observer assessments of patient appearance 3 and 6 hours postoperatively. Forty percent of patients who received diclofenac were awake and calm 3 hours postoperatively, compared to none in the other groups. Fifty-five percent of patients in group A compared to 10% in the other groups were awake and

calm at 6 hours. An improvement in behaviour at this stage offers a potential reduction in the demand placed upon the vigilance of nursing staff in the detection of possible respiratory obstruction in the sleeping child. The incidence of side effects was not significantly different between diclofenac and both other groups.

A further point in favour of diclofenac is its minimal effect upon respiratory rate. There was no significant decrease in respiratory rate in group A at any assessment on the day of operation compared to that recorded the following morning. Respiratory rates in patients who received papaveretum, were significantly lower than in the diclofenac group 1 and 3 hours postoperatively, and also lower than the rates recorded at 24 hours when any respiratory depressant action of the opioid analgesic could be considered to be negligible.

The use of suppositories in the United Kingdom is not widely practised.⁸ However, it carries the advantage of the possible avoidance of the 'first pass' effect.⁹ NSAIDS when taken orally may cause dyspepsia, gastric erosions or haemorrhage. The use of suppositories may reduce these side effects although it will not necessarily avoid them, since irritation depends not only on a local action in the stomach but also on the plasma concentration of the drug.¹⁰ The children were unaware of the route of administration of the drugs and no problems were noted with the administration of the suppositories. No parent declined to allow their child to enter into the study because of the possible use of a suppository. Diclofenac is absorbed rapidly and completely after oral, rectal or intramuscular administration to man.¹¹ Elimination is rapid; 90% clearance takes 3-4 hours and the drug and its metabolites are excreted in urine and bile.

Dommerby and Rasmussen⁴ compared the use of diclofenac with no analgesia in an older population of children who underwent tonsillectomy, and found it to offer good pain relief. However, in that study the greater postoperative consumption of paracetamol in the group that received no analgesia could be anticipated. Satisfactory analgesia in the early postoperative period can be achieved by premedication with an opioid. However, logistical problems of the correct timing of premedication, and the fear of injections by young children, preclude the widespread use of this method. Opioids administered intra-operatively carry the potential disadvantage of unpredictable respiratory depression during spontaneous ventilation with the use of a volatile agent. The replacement by a potent analgesic without respiratory depressant effects, offers considerable advantages and serves to counteract the arguments of those who would rather withhold analgesia at this time.

antages and serves to counteract the arguments of those who would rather withhold analgesia at this time.

In conclusion, this study demonstrates that the use of rectal diclofenac intra-operatively during anaesthesia for tonsillectomy produces postoperative analgesia comparable to that provided by papaveretum given either intra-operatively or immediately postoperatively. However, diclofenac offers the advantages of less respiratory depression, less requirement for postoperative paracetamol and a patient who is awake and calm at an earlier time postoperatively. This drug may offer advantages over papaveretum with regard to safety and convenience when used in this way.

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References

1. HANNINGTON-KIFF JG. The need for analgesia cover after ENT surgery - comparison of nefopam and papaveretum. *Anaesthesia* 1985; **40**: 76-8.
2. SAARNIVAARA L, METSA-KETELA T, MANNISTO P, VAPAATALO H. Pain relief and sputum prostaglandins in adults treated with pethidine, tilidine and indomethacin after tonsillectomy. A double-blind study. *Acta Anaesthesiologica Scandinavica* 1980; **24**: 79-85.
3. REASBECK PG, RICE ML, REASBECK JC. Double-blind controlled trial of indomethacin as an adjunct to narcotic analgesia after major abdominal surgery. *Lancet* 1982; **2**: 115-8.
4. DOMMERBY H, RASMUSSEN OR. Diclofenac (Voltaren). Pain-relieving effect after tonsillectomy. *Acta Oto-laryngologica (Stockholm)* 1984; **98**: 185-92.
5. BRAMWELL RGB, BULLEN C, RADFORD P. Caudal block for postoperative analgesia in children. *Anaesthesia* 1982; **37**: 1024-8.
6. KRISHNAN A, TOLHURST-CLEAVER CL, KAY B. Controlled comparison of nalbuphine and morphine for post-tonsillectomy pain. *Anaesthesia* 1985; **40**: 1178-81.
7. REVILL SI, ROBINSON JO, ROSEN M, HOGG MIJ. The reliability of linear analogue for evaluating pain. *Anaesthesia* 1976; **31**: 1191-8.
8. Suppositories for systemic medication: an underused approach. *Drug and Therapeutics Bulletin*. 1983; **21**: 53-6.
9. DE BOER AG, MOOLENAAR F, DE LEEDE LGJ, BREIMER DD. Rectal drug administration: clinical pharmacokinetic considerations. *Clinical Pharmacokinetics* 1982; **7**: 285-311.
10. BABER N, SIBEON R, LAWS E, HALLIDAY L, ORME M, LITTLER T. Indomethacin in rheumatoid arthritis: comparison of oral and rectal dosing. *British Journal of Clinical Pharmacology* 1980; **10**: 387-92.
11. JOHN VA. The pharmacokinetics and metabolism of diclofenac sodium (Voltarol) in animals and man. *Rheumatology and Rehabilitation* 1979; Suppl. **2**: 22-37.

Nalbuphine combined with midazolam for outpatient sedation

An assessment of safety in volunteers

M. R. J. SURY AND P. V. COLE

Summary

Eighteen healthy volunteers were studied in a double-blind trial to determine which dose of nalbuphine (0.05, 0.1 or 0.2 mg/kg) may be combined with midazolam 0.05 mg/kg to provide a safe outpatient intravenous sedative technique. The ventilatory response to carbon dioxide and end tidal PCO_2 were measured before and after the drugs were administered. A mild degree of respiratory depression occurred, which was maximal at 3–30 minutes after injection. This was not related to dose except that nalbuphine 0.05 mg/kg resulted in the slowest respiratory rates. The implications of these findings for clinical practice are discussed.

Key words

Analgesics, narcotic; nalbuphine.

Hypnotics, benzodiazepines; midazolam.

The large increase in popularity of day case surgery¹ has produced a strong demand for improved sedation from both patients and clinicians. A perfect sedative technique has yet to be found. Intravenous benzodiazepines provide sedation with amnesia and, within limits, will cause minimal cardiovascular and respiratory disturbance. However, some surgical procedures are so painful that large doses of drugs are required to control the patient and, even then, their success can rely heavily on amnesic properties.² The addition of an analgesic to a benzodiazepine reduces the doses required of both drugs and improves the comfort of the patient.^{3,4}

The patient is still exposed to the risk of respiratory depression despite these benefits. Nalbuphine is a new partial agonist opioid which, in comparison with pentazocine, has a lower incidence of nausea, vomiting and psychomimetic effects.⁵ The combination of nalbuphine with a water-soluble benzodiazepine may provide an improved technique.

We therefore attempted to determine the nalbuphine dose which may safely be combined with midazolam by measuring the degree of respiratory and cardiovascular depression, if any, in healthy volunteers.

of three groups: group A ($n = 6$), nalbuphine 0.05 mg/kg plus midazolam 0.05 mg/kg; group B ($n = 6$), nalbuphine 0.1 mg/kg plus midazolam 0.05 mg/kg; or group C ($n = 6$), nalbuphine 0.2 mg/kg plus midazolam 0.05 mg/kg.

All subjects were healthy, had no history of drug hypersensitivity and had received no medication in the previous 2 weeks. Each subject gained familiarity with the test equipment before the experiment and was instructed to fast overnight and to abstain from alcohol. On the morning of the experiment a 23-gauge cannula was inserted into a vein and an ECG and sphygmomanometer attached. The volunteer then remained supine until the end of the study. Baseline measurements were taken after 30 minutes of undisturbed rest, and the midazolam and nalbuphine were injected 10 minutes later (each over one minute). The ventilatory response to carbon dioxide and resting end tidal carbon dioxide ($Pe'CO_2$) were measured at baseline and at 3, 15, 30, 60 and 120 minutes after the drugs. Pulse and respiratory rates together with arterial blood pressures and sedation scores (Table 1) were recorded at regular intervals throughout the experiment. Amnesia and ability to walk a

Methods

This study was approved by the District Ethical Committee and all subjects gave informed, written consent. Eighteen volunteers were allocated in a double-blind manner to one

Table 1. Sedation scores.

0, wide awake
1, slight drowsiness
2, marked drowsiness but responds to spoken word
3, asleep, responds to physical stimuli but not to spoken word
4, asleep, no response to spoken word or physical stimuli

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straight line were assessed after 2 hours and any side effects noted.

The ventilatory response to carbon dioxide was measured using a modified rebreathing method.⁶ The subject, wearing a nose clip, breathed into a wet drum spirometer which had previously been filled with 5% carbon dioxide in oxygen to a volume of 8–10 litres. The spirometer was modified to give an analogue electrical output which was displayed on a chart recorder, and from which minute volume could be calculated for each single breath. $PE'CO_2$ was measured continuously from the mouthpiece by a PK Morgan 901 Mk 2 capnograph and the waste gas was returned to the closed system. The analogue output from the capnograph was displayed on the second channel of the recorder. The spirometer was calibrated with a standard 2-litre syringe and the capnograph with known carbon dioxide concentrations (Alpha Standard, BOC). Room temperature and pressure were determined for each test and used to convert all volumes to BTPS and end expired CO_2 concentrations (%) to $PE'CO_2$ (kPa).

The resting $PE'CO_2$ was measured before the carbon dioxide response test and the prepared rebreathing system was subsequently attached at the end of an expiration. The volunteer was then left undisturbed for 4 minutes while $PE'CO_2$ increased to approximately 8%. The carbon dioxide response was calculated by graphically plotting minute volume against coincident $PE'CO_2$ and calculating the gradient of the linear relationship using the method of least squares.

All data were normally distributed and paired *t*-tests and one-way analysis of variance (ANOVA) were applied to determine the significance of changes from baseline in each group and differences between the groups. A *p* value < 0.05 was taken as significant.

Results

Subjects' ages ranged from 25–35 years and their weights from 50–82 kg. Carbon dioxide response measurements were made on 108 occasions, but six were excluded because of mechanical problems and four because of poor correlation (Table 2). There was a trend for the carbon dioxide response to decrease following the injection of the drugs. Paired *t*-tests showed significant mean percentage changes from baseline for all groups (Table 3). One-way ANOVA failed to demonstrate a difference between the groups.

End tidal carbon dioxide levels tended to increase at 3, 15 and 30 minutes and then return to near normal by 60 minutes (Fig. 1). One-way ANOVA did not demonstrate a difference between the groups. At no time did $PE'CO_2$ exceed 7 kPa and usually not 6.5 kPa.

A short period of apnoea (always less than 20 seconds) occurred soon after the drugs were injected but respiratory rates decreased to 6 breaths/minute only on two occasions. Group B alone had significant decreases in respiratory rate with time, although group A had overall lower values than the other two groups ($F = 6.55$). Pulse rate and arterial blood pressure did not change significantly with time, or between groups. Maximum sedation tended to occur at 3 minutes and full awareness always returned by 120 minutes (Table 4). There were no significant differences between the groups. One volunteer in each of groups A and C required temporary support of the mandible to allow the carbon dioxide tests to be successful. Sixteen out of the 18

Table 2. Carbon dioxide response data for groups A, B and C. Gradients of individual carbon dioxide response lines (litres/minute/kPa) and group means (SEM) are presented against baseline and time (minutes) following injection of drugs.

Baseline	Time after injection, minutes				
	3	15	30	60	120
Group A					
10.2	9.2	8.0	4.9	5.2	7.4
11.4	—	5.0	9.6	6.3	7.5
9.4	3.7	8.6	9.9	8.7	6.8
9.2	4.5	7.1	6.2	—	7.1
10.1	8.7	11.3	6.5	8.1	7.6
6.9	5.5	7.8	5.6	—	5.5
Mean	9.53	6.32	7.97	7.12	7.1
	(0.61)	(1.11)	(0.84)	(0.86)	(0.83)
	(0.32)				
Group B					
8.3	—	3.8	10.3	—	2.7
13.1	18.6	18.6	—	15.8	—
16.5	8.1	8.0	9.8	26.5	4.8
8.6	8.9	7.8	10.0	6.0	7.3
22.9	7.2	5.8	4.6	12.8	8.5
14.0	7.6	6.2	7.8	10.0	5.6
Mean	13.9	10.08	8.37	8.5	14.22
	(2.22)	(2.15)	(2.14)	(1.07)	(3.47)
					(1.01)
Group C					
9.7	—	—	—	5.2	2.4
11.8	18.0	12.0	3.2	11.0	8.3
12.7	18.6	13.7	12.7	12.7	9.1
31.8	17.8	21.7	20.5	19.2	19.8
18.2	18.4	13.3	13.4	13.7	15.7
20.6	10.6	7.0	9.9	8.9	5.9
Mean	17.47	16.68	13.54	11.94	11.78
	(3.32)	(1.52)	(2.37)	(2.80)	(1.93)
					(2.63)

—, Excluded measurement (see Results).

Table 3. Carbon dioxide response data expressed as percentage change from baseline. Mean (SEM) gradients for groups A, B and C are presented against time (minutes) following injection of drugs, and for all times.

	Time after injection, minutes					All times
	3	15	30	60	120	
<i>Group A</i>						
-31	-14	-25	-30	-26	-25**	
(10.3)	(10.6)	(8.2)	(10)	(2)	(3)	
<i>Group B</i>						
-24	-34	-25	-4	-55	-28*	
(20.6)	(17.6)	(19.7)	(19.7)	(10.3)	(8.3)	
<i>Group C</i>						
-2	-23	-37	-29	-43	-27*	
(21.5)	(13.4)	(12.1)	(9.4)	(10.2)	(7.1)	

* *p* < 0.05, ** *p* < 0.01, significant mean percentage change from baseline.

Table 4. Mean sedation scores (see Table 1) taken at baseline and various times (minutes) following injection of nalbuphine with midazolam.

Baseline	Time, minutes								
	3	15	30	45	60	75	90	105	120
Group A									
0	2	1.5	1.5	1	0.83	0.83	0.5	0.5	0.17
Group B									
0	1.67	1.5	1	1	0.66	0.5	0.66	0.66	0
Group C									
0	2	1.5	1.17	1	0.83	0.85	0.5	0.33	0.17

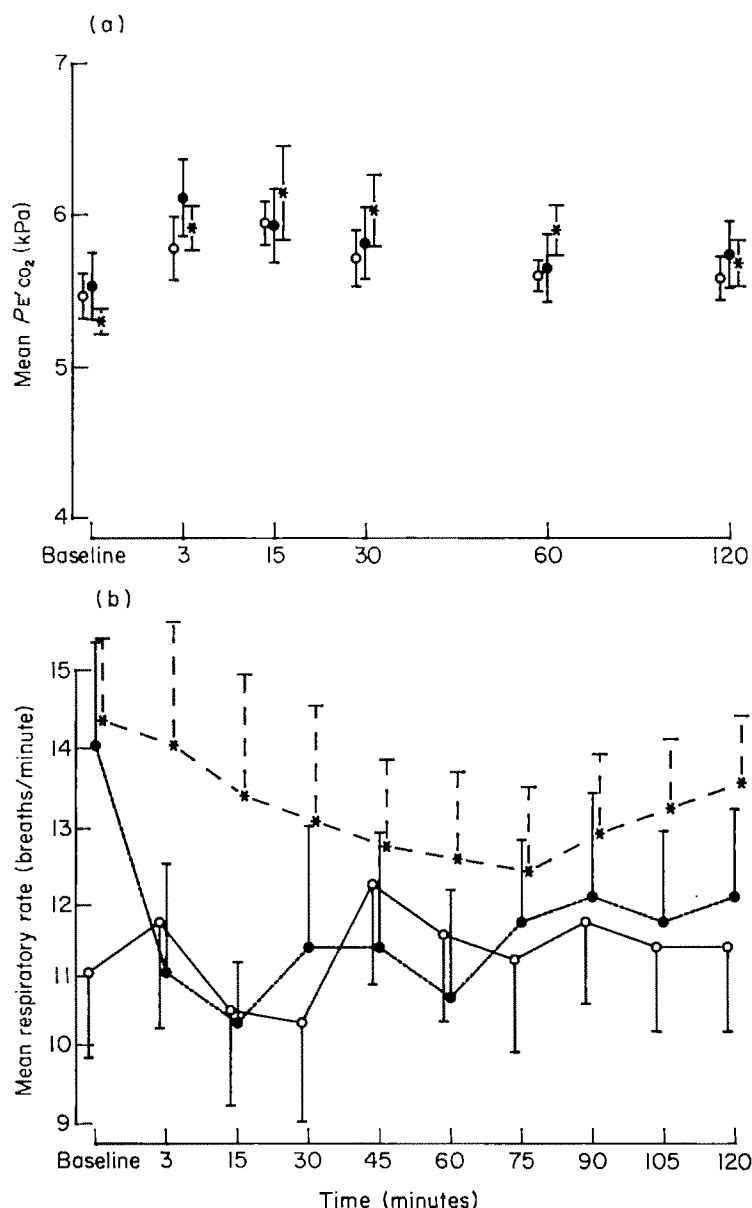


Fig. 1. (a) Mean (SEM) $PE'CO_2$ and (b) mean respiratory rates, shown against baseline and time elapsed following injection of nalbuphine with midazolam 0.05 mg/kg. ○, Nalbuphine 0.05 mg/kg; ●, nalbuphine 0.1 mg/kg; *, nalbuphine 0.2 mg/kg.

volunteers had profound amnesia for part of the study. Subjects were not nauseated while supine but six experienced nausea and one vomited after walking. Everyone was able to walk unaided 2 hours after the drugs but three volunteers required an extra period of rest because of movement-related nausea. Dreams and hallucinations were not recalled except for one subject who had an unpleasant hypnopompic sensation several hours later at home. All but four volunteers felt tired on the evening following the drugs; nevertheless, all agreed that their sedation was pleasant while they were supine.

Discussion

The combination of a benzodiazepine with an opioid should theoretically prove to be an ideal sedative technique for day case surgery. Diazepam has largely been superseded

by midazolam because of the latter's more rapid action, shorter half-life and the absence of a second peak phenomenon.^{7,8} It also has the advantage that it causes minimal local venous sequelae and profound amnesia.^{9,10} High doses are needed to provide sedation if the opioids are administered alone and, consequently, respiratory depression, nausea and psychotomimetic side effects can result.¹¹ Nalbuphine, when used in doses of 0.1–0.2 mg/kg, has analgesic and respiratory depressant properties similar to those of morphine.^{12,13} However, a ceiling effect of respiratory depression has been observed when higher doses are given and this provides a measure of safety for accidental overdose.¹⁴ Other advantages include cardiovascular stability¹⁵ and, in comparison with pentazocine, a low incidence of side effects.¹⁶ The nalbuphine-midazolam combination has already been used with success in dental surgery and is accepted widely by patients because of a low incidence of side effects and a short recovery period.¹⁷

Severe respiratory depression was not observed in our study (none of the volunteers exceeded a $Pe'CO_2$ of 7 kPa) but minor respiratory changes were noted immediately following injection and for up to 2 hours thereafter. Subjects were always rousable and low respiratory rates (6 breaths/minute was recorded only twice throughout) and single short apnoeic periods were not considered dangerous.

The carbon dioxide response test has often been used in drug trials but, unfortunately, interpretation of the results has been handicapped by large between- and within-subject variability.¹⁸ Some previous workers attempted to overcome these problems by use of changes from baseline data,¹⁹ whilst others have favoured simple measurement of $Pe'CO_2$ as a more sensitive technique.^{12,18} Morphine is known to cause a decrease in carbon dioxide response gradient of 47%²⁰ and this compares favourably with our result of 25–28% (Table 2). The nalbuphine–midazolam combination caused a mean increase in $Pe'CO_2$ of 0.56 kPa compared with an increase of 0.47 kPa in a previous morphine study in awake volunteers.²¹

In our study changes in $Pe'CO_2$ and carbon dioxide response (Fig. 1) with time indicate that maximum respiratory depression occurred 3 and 30 minutes after injection of the drugs and clinicians therefore should remain alert to this problem. Other features of the drug combination were pleasant sedation and cardiovascular stability but the appreciable incidence of movement-related nausea (33%) was unexpected. The findings of this study should be applied to everyday clinical practice with caution, since patients are frequently neither young nor healthy and commonly have chronic chest disease. Furthermore, results from volunteers who were left undisturbed may not predict results from a clinical trial because, by comparison, patients will be in relative discomfort in a noisy operating theatre.

In conclusion, all the doses of nalbuphine (0.05, 0.1 and 0.2 mg/kg) were safe in volunteers when combined with midazolam 0.05 mg/kg and this mixture appears to be eminently suitable for a clinical trial.

Acknowledgments

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References

1. Commission on the provision of surgical services. *Guide lines for day case surgery*. Royal College of Surgeons of England, July 1985.
2. DUNDEE JW. Abuse of benzodiazepines. *British Journal of Anaesthesia* 1983; **55**: 1–2.
3. CORALL IM, STRUNIN L, WARD ME, MASON SA, ALCALAY M. Sedation for outpatient conservative dentistry. A trial of pentazocine supplementation to diazepam and local analgesia techniques. *Anaesthesia* 1979; **34**: 855–8.
4. MURRAY-LAWSON JI, MILNE MK. Intravenous sedation with diazepam and pentazocine. A study in dosage. *British Dental Journal* 1981; **151**: 379–80.
5. ERRICK JK, HEEL RC. Nalbuphine: a preliminary review of its pharmacological properties and therapeutic efficacy. *Drugs* 1983; **26**: 191–211.
6. READ DJC. A clinical method for assessing the ventilatory response to carbon dioxide. *Australian Annals of Medicine* 1967; **16**: 20–32.
7. DUNDEE JW, SAMUEL IO, TONER W, HOWARD PJ. Midazolam: a water-soluble benzodiazepine. Studies in volunteers. *Anaesthesia* 1980; **35**: 454–8.
8. WHITWAM JG, AL-KHUDHAIRI D, MCCLOY RF. Comparison of midazolam and diazepam in doses of comparable potency during gastroscopy. *British Journal of Anaesthesia* 1983; **55**: 773–6.
9. BERGGREN L, ERIKSSON I, MOOLENHOLT P, WICKBOM G. Sedation for fiberoptic gastroscopy: a comparative study of midazolam and diazepam. *British Journal of Anaesthesia* 1983; **55**: 289–96.
10. MIKKELSEN M, HOEL TM, BRYNE H, KROHN CD. Local reactions after injections of diazepam, flunitrazepam and isotonic saline. *British Journal of Anaesthesia* 1980; **52**: 817–9.
11. BROWN PRH, DONALDSON D, GRAY IG, MAIN DMG. Intravenous sedation in dentistry: a comparative study of diazepam and pentazocine. *Dental Practitioner and Dental Record* 1970; **21**: 2–6.
12. KLEPPER ID, ROSEN M, VICKERS MD, MAPLESON WW. Respiratory function following nalbuphine and morphine in anaesthetized man. *British Journal of Anaesthesia* 1986; **58**: 625–9.
13. GAL TJ, DiFAZIO CA, MOSCICKI J. Analgesic and respiratory depressant activity of nalbuphine: a comparison with morphine. *Anesthesiology* 1982; **57**: 367–74.
14. ROMAGNOLI A, KEATS AS. Ceiling effect for respiratory depression by nalbuphine. *Clinical Pharmacology and Therapeutics* 1980; **27**: 478–85.
15. LEE G, LOW RI, AMSTERDAM EA, DEMARIA AN, HUBER PW, MASON DT. Hemodynamic effects of morphine and nalbuphine in acute myocardial infarction. *Clinical Pharmacology and Therapeutics* 1981; **29**: 576–81.
16. TAMMISTO T, TIGERSTEDT I. Comparison of the analgesic effects of intravenous nalbuphine and pentazocine in patients with postoperative pain. *Acta Anaesthesiologica Scandinavica* 1977; **21**: 390–4.
17. PARSONS JD. The use of nalbuphine (nubain) and midazolam in sedation for dentistry. *Society for the Advancement of Anaesthesia in Dentistry Digest* 1986; **6**: 125–31.
18. JENNETT S. Assessment of respiratory effects of analgesic drugs. *British Journal of Anaesthesia* 1968; **40**: 746–56.
19. POWER SJ, MORGAN M, CHAKRABARTI MK. Carbon dioxide response curves following midazolam and diazepam. *British Journal of Anaesthesia* 1983; **55**: 837–41.
20. CORMACK RS, MILLEDGE JS, HANNING CD. Respiratory effects and amnesia after premedication with morphine or lorazepam. *British Journal of Anaesthesia* 1977; **49**: 351–60.
21. JENNETT S, BARKER JG, FORREST JB. A double-blind controlled study of the effects on respiration of pentazocine, phenoperidine and morphine in normal man. *British Journal of Anaesthesia* 1968; **40**: 864–75.

Nalbuphine combined with midazolam for outpatient sedation

An assessment in fiberoptic bronchoscopy patients

M. R. J. SURY AND P. V. COLE

Summary

Forty patients who required day case fiberoptic bronchoscopy were sedated with either nalbuphine 0.2 mg/kg and midazolam 0.05 mg/kg ($n = 20$), or midazolam 0.05 mg/kg alone ($n = 20$). Extra midazolam was administered when required. The degree of respiratory depression measured by arterialised venous carbon dioxide levels was recorded together with heart rate, arterial blood pressure, respiratory rate and sedation score, before administration of the drugs and at regular intervals thereafter. Patients who received nalbuphine had slightly higher carbon dioxide levels but respiratory rate and cardiovascular changes were similar in both groups. The addition of nalbuphine to midazolam improves the quality of sedation but prolongs the recovery time and increases the incidence of side effects.

Key words

Anaesthesia; outpatient.

Analgesics, narcotic; nalbuphine.

Hypnotics, benzodiazepines; midazolam.

The management of patients who require painful procedures has been improved by the addition of an analgesic to benzodiazepine sedative techniques.^{1,2} Nalbuphine 0.2 mg/kg combined with midazolam 0.05 mg/kg did not cause appreciable respiratory or cardiovascular depression in a previous study of healthy volunteers.³ This clinical trial compares the safety and efficacy of this combination with midazolam alone to sedate patients who undergo day case fiberoptic bronchoscopy.

Methods

Forty patients who required day case fiberoptic bronchoscopy were sedated in a randomised double-blind manner with either intravenous midazolam alone (group A, $n = 20$) or in combination with nalbuphine (group B, $n = 20$). The study was approved by the District Ethical Committee and each patient gave written, informed consent.

All patients were fasted overnight and were unpremedicated. A 23-gauge cannula was placed in a vein on the dorsum of the hand which was warmed to 40°C by a small electric blanket. Glycopyrronium 0.2 mg was given intravenously and ECG electrodes and sphygmomanometer cuff were attached. Nalbuphine 0.2 mg/kg or normal saline was then injected slowly over 30 seconds and, 2 minutes later, midazolam 0.05 mg/kg (or 0.04 mg/kg if weight < 50 kg or

age > 65 years) was given. The patient's nose and pharynx were sprayed with 4% lignocaine and the fiberoptic bronchoscope inserted, usually through the nose. Further topical analgesia was given via the bronchoscope. Bronchoscopy took between 10 and 30 minutes and extra sedation was provided by increments of midazolam 0.5–1 mg if requested by the operator.

Pulse rate, arterial blood pressure and respiratory rate were recorded at the following times: before drug administration; 3 minutes after drug administration; during bronchoscopy, approximately 15 minutes later; shortly after the procedure; and 2 hours later, in the recovery ward. Carbon dioxide tensions were measured in venous blood samples collected from the warmed back of hand without the use of a tourniquet,^{4,5} before and 3 minutes after the drugs were given and again 15 minutes later during bronchoscopy. Sedation was also assessed at the above times using a numerical scoring system (Table 1), and observations of the global efficacy of sedation and side effects were also noted. Amnesia for the procedure and the ability to walk a straight line were assessed at 2 hours.

Student's *t*-test and Mann–Whitney *U*-tests were applied to determine the difference between the groups. Where multiple measurements were taken over the experimental period the mean change from baseline was calculated for individual patients. Significant difference implies $p < 0.05$.

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Table 1. Sedation and global efficacy scores.

Sedation	
0,	wide awake
1,	slight drowsiness
2,	marked drowsiness but responds to spoken word
3,	asleep, no response to spoken word
4,	asleep, no response to spoken word or physical stimuli
Global efficacy	
0,	patient too sedated and not responsive to command
1,	patient relaxed, calm, cooperative and does not resist procedure
2,	patient slightly restless and shows mild resistance
3,	patient very restless and shows active resistance

Table 2. Distributions of age, weight and sex for groups A and B.

	Group A (midazolam only)	Group B (midazolam and nalbuphine)
Mean (SEM) age, years	58.3 (2.9)	54.9 (3.9)
Mean (SEM) weight, kg	69.9 (3.2)	68.3 (3.4)
Sex, M/F	16/4	14/6

Patients

There were no significant differences between the two groups for age, weight or sex (Table 2). Five patients in each group had chronic obstructive airways disease as demonstrated by either clinical examination, forced expiratory volume (in 1 second) <75% of the vital capacity, or peak expiratory flow rate of <350 litres/minute. One patient in group B was currently treated for bronchospasm with prednisolone and another with a salbutamol inhaler. Other patients had minor features of chronic lung disease but all had sufficient respiratory reserve to climb a single flight of stairs. In each group one patient had ischaemic heart disease controlled with nifedipine, oxprenolol and glyceryl trinitrate. There were three hypertensive patients in group B and one in group A, and all were treated adequately with β -adrenoceptor blockers, diuretics or methyldopa. Three patients in group B had mild congestive heart failure treated with small doses of diuretics. One patient in each group had non insulin-dependent diabetes treated with glibenclamide.

Results

Five patients in group A and one in group B required extra midazolam to make bronchoscopy tolerable. Sedation was significantly greater following the combination of drugs than after midazolam alone (Fig. 1; $p = 0.025$). Patients were able to respond to verbal commands at all times except just after the injection of the drugs, when one patient in group A (age 78 years) and two in group B (ages 60 and 66 years) were rousable with gentle physical stimuli. The global efficacy scores were significantly lower (i.e. patients were more comfortable) after midazolam and nalbuphine (Fig. 2; $p = 0.018$).

Venous carbon dioxide levels tended to increase slightly after the drug combination although they decreased significantly after midazolam alone (Fig. 3). The mean increase in venous carbon dioxide tension in group B was 0.15 kPa. Respiratory rates were similar in both groups and

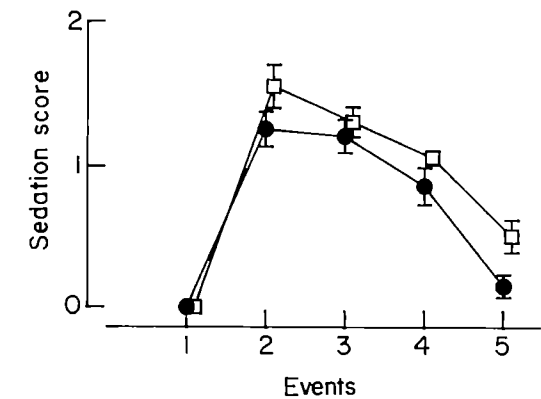


Fig. 1. Sedation scores (see Table 1) recorded at various times during fibreoptic bronchoscopy. Group A (●) received midazolam only and group B (□) received nalbuphine and midazolam. The events are as follows: 1, before drugs; 2, 3 minutes after drugs; 3, during bronchoscopy, approximately 15 minutes later; 4, shortly after the procedure; 5, 2 hours later, in the recovery ward. Significant difference ($p = 0.025$) between groups in the mean change from baseline values.

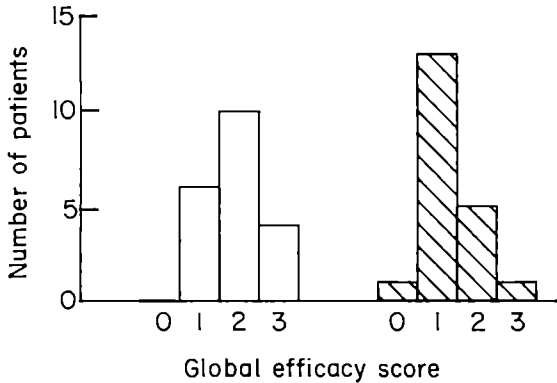


Fig. 2. Global efficacy scores (see Table 1) of sedation for patients sedated during fibreoptic bronchoscopy. Group A (□) received midazolam only and group B (▨) received nalbuphine and midazolam. Significant difference ($p = 0.018$) between groups in the mean change from baseline values.

always remained above 10 breaths/minute (Fig. 3). Three patients showed clinical features of respiratory depression but none required supportive treatment. One patient (71 years) in group A had an apnoeic period of 30 seconds, and two (aged 59 and 61 years) in group B had minor obstructive apnoea but all three were roused easily. Appreciable cardiovascular depression was not observed and there were no differences between the groups for heart rate or arterial pressure (Fig. 3). However, heart rate and blood pressure were significantly higher during bronchoscopy itself than at any other time.

Two hours after the drugs were injected there were obvious differences in recovery scores between the groups. Seven patients who received nalbuphine were unable to walk unaided at 2 hours, compared with two who did not receive the narcotic. Nausea was related to movement and occurred only during the recovery period, in four patients in group B and in one in group A.

Six patients in group B complained of dizziness just after the nalbuphine and three in group A complained of mild headache. The injection of nalbuphine was always painless. There were no significant differences in amnesia between

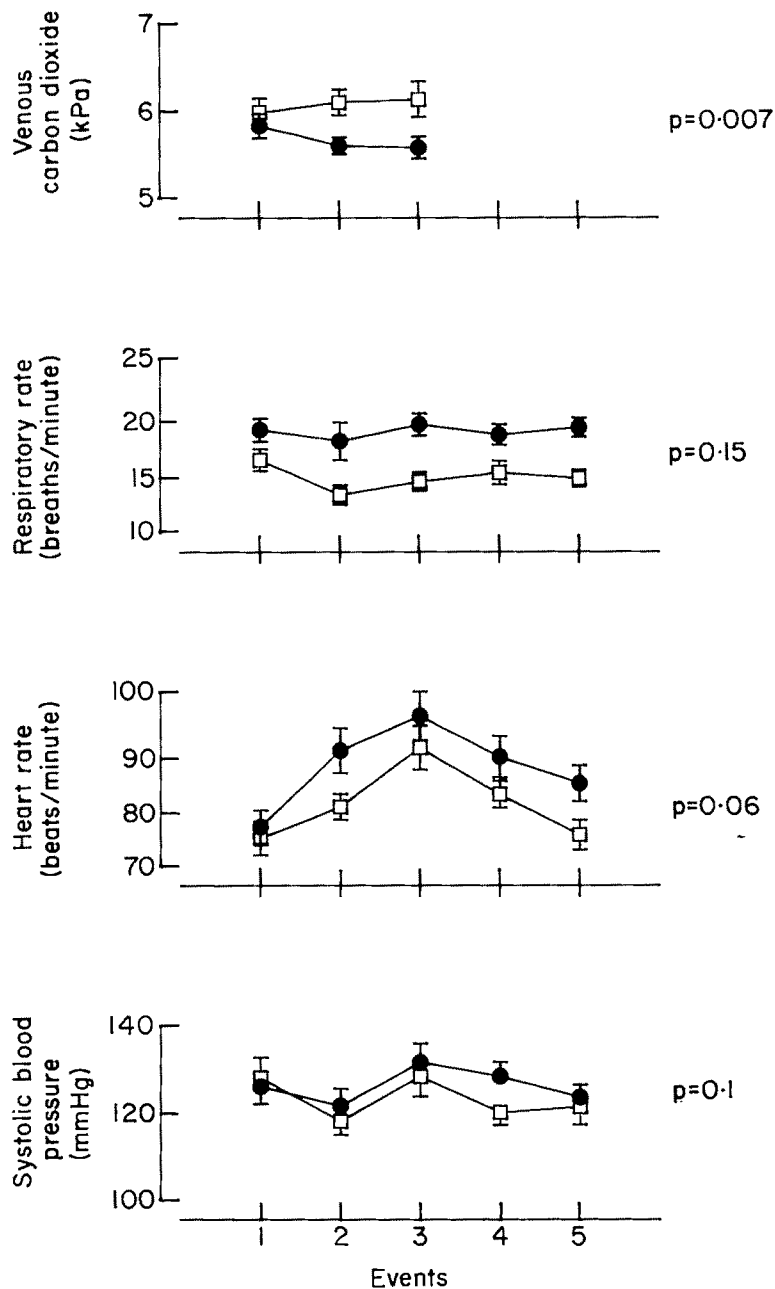


Fig. 3. Venous carbon dioxide levels, respiratory rates, heart rates and systolic blood pressures (mean, SEM) of patients in groups A and B measured at various times during fiberoptic bronchoscopy (see legend to Fig. 1). Patients in group A (●) received midazolam only and those in group B (□) received nalbuphine and midazolam. Values of *p* represent significant differences between groups in the mean changes from baseline values.

the two groups; five patients in group A and four in group B had full recall of events.

Discussion

The combination of nalbuphine 0.2 mg/kg with midazolam provided a safe and successful sedative technique in this clinical trial. The degree of respiratory depression measured by venous carbon dioxide levels,^{4,5} was minimal and the changes in respiratory rate, pulse rate and blood pressure were similar to those recorded during sedation with midazolam alone. Comparison of the sedation and global efficacy scores shows that nalbuphine markedly increased

patient comfort during bronchoscopy, but these improvements were achieved at the risk of nausea, dizziness and prolonged recovery. Furthermore, two patients in the nalbuphine group had obstructive apnoea, and the sedative properties of nalbuphine may increase the risk of excessive sedation.

Nalbuphine has proved to be a particularly valuable analgesic component of sedation in dentistry,^{6,7} especially when satisfactory operating conditions are not readily achieved by benzodiazepines alone. Nevertheless, its disadvantages must be borne in mind if recovery facilities are limited.

In conclusion, sedation with nalbuphine-midazolam com-

bination should be reserved for prolonged painful procedures when benzodiazepines alone are inadequate, and we emphasise the need for full resuscitation and recovery facilities.

Acknowledgments

This study was supported by Du Pont (UK) Limited. We are grateful to Mrs P. Patel, who provided statistical analysis.

References

1. CORALL IM, STRUNIN L, WARD ME, MASON SA, ALCALAY M. Sedation for outpatient conservative dentistry. A trial of pentazocine supplementation to diazepam and local analgesia techniques. *Anaesthesia* 1979; 34: 855-8.
2. MURRAY-LAWSON JI, MILNE MK. Intravenous sedation with diazepam and pentazocine. A study in dosage. *British Dental Journal* 1981; 151: 379-80.
3. SURY MRJ, COLE PV. Nalbuphine combined with midazolam for outpatient sedation: an assessment of safety in volunteers. *Anaesthesia* 1988; 43: 281-284.
4. FORSTER HV, DEMPSEY JA, THOMPSON J, VIDRUK E, DOPICO GA. Estimation of arterial PO_2 , PCO_2 , pH, and lactate from arterialized venous blood. *Journal of Applied Physiology* 1972; 32: 134-7.
5. BROOKS D, WYNN V. Use of venous blood for pH and carbon-dioxide studies, especially in respiratory failure and during anaesthesia. *Lancet* 1959; 1: 227-30.
6. HUNTER PL. The use of nalbuphine (nubain) for analgesia in combination with methohexitone sodium. *Journal of the Society for the Advancement of Anaesthesia in Dentistry* 1986; 6: 100-2.
7. PARSONS JD. The use of nalbuphine (nubain) and midazolam in sedation for dentistry. *Journal of the Society for the Advancement of Anaesthesia in Dentistry* 1986; 6: 125-31.

Continuous epidural infusion of 0.075% bupivacaine for pain relief in labour

A comparison with intermittent top-ups of 0.5% bupivacaine

J. A. HICKS, J. G. JENKINS, M. C. NEWTON AND I. L. FINDLEY

Summary

Seventy-three women who requested epidural analgesia during labour were randomly allocated in a prospective study to receive either a continuous epidural infusion of 0.075% bupivacaine at a rate of 12–18 ml/hour (38 mothers) or intermittent top-ups of 0.5% bupivacaine (35 mothers). Both groups received an initial dose of 6–8 ml bupivacaine 0.5%. Patients were asked to score their pain using a 10-cm linear scale prior to insertion of the epidural, 30 minutes after its insertion and hourly thereafter. The quality of analgesia in the continuous infusion group was significantly better than in the intermittent top-up group ($p < 0.025$). There was no significant difference in the total dose of bupivacaine given to the two groups.

Key words

Anaesthetic techniques, regional; epidural.

Anaesthetics, local; bupivacaine.

There has been considerable interest recently in the use of continuous epidural infusions for pain relief in labour. Most previous studies^{1–9} have used continuous epidural infusions of either 0.125% or 0.25% bupivacaine, although recently Ewen *et al.*¹⁰ showed 0.08% bupivacaine to be superior to infusions of 0.25% bupivacaine. No study has compared the quality of analgesia provided by a continuous infusion of low concentration bupivacaine with that provided by a standard regimen of intermittent top-ups. We therefore conducted a prospective randomised trial that compared a continuous epidural infusion of 0.075% bupivacaine with intermittent top-ups of 0.5% bupivacaine.

Methods

Seventy-three women aged between 16 and 35 years who requested epidural analgesia during labour were included in the study, which was approved by the local ethical committee. The nature and risks of the procedure were explained to the patient and written consent obtained. Patients were randomly allocated to one of two groups; the top-up group received intermittent top-ups of 0.5% bupivacaine, and the infusion group a continuous epidural infusion of 0.075% bupivacaine. No other analgesic or sedative drugs were given. The following groups were not eligible for inclusion

in the trial: gestational age less than 36 weeks, multiple pregnancy, breech presentation, probable cephalopelvic disproportion, trial of scar, the presence of moderate or severe hypertension or pre-eclampsia, cervical dilatation greater than 8 cm, coagulation defect or local sepsis.

The mother's circulation was preloaded with 500 ml Hartmann's prior to insertion of the epidural and the arterial blood pressure recorded. The mother was asked to score her pain using a 10-cm linear scale. This was a horizontal line labelled 'no pain' at one extreme and 'worst pain imaginable' at the other. The epidural space was located with the mother in the left lateral position, at either the L_{2/3} or L_{3/4} interspace with a 16-gauge Tuohy needle using loss of resistance to either saline or air. An epidural catheter was advanced through the Tuohy needle and 3 cm left in the epidural space. The epidural was resited in a different interspace if a bloody tap occurred, and the mother continued in the study. A test dose of 2 ml bupivacaine 0.5% was given after a negative aspiration test for cerebrospinal fluid and blood. A further 4–6 ml bupivacaine 0.5% was given if there were no untoward sequelae 5 minutes after the test dose. The patient was then turned onto her right side and the arterial pressure recorded every 5 minutes for 20 minutes.

The epidural in the top-up group was topped up by the midwife with 6–8 ml bupivacaine 0.5% on maternal request.

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The mother was positioned as necessary and the arterial pressure recorded every 5 minutes for 20 minutes after each top-up. A top-up of up to 10 ml bupivacaine 0.5% was given in the sitting position if analgesia was required for instrumental delivery.

A continuous epidural infusion of 0.075% bupivacaine at a rate of 15 ml/hour was started in the infusion group 30 minutes after the initial dose of 0.5% bupivacaine. The solution was prepared by dilution of 7.5 ml bupivacaine 0.5% in 0.9% saline to a volume of 50 ml. The infusion was via a Vickers IP5 syringe pump. The arterial pressure was recorded every 5 minutes for 20 minutes after the start of the infusion and hourly thereafter. No posturing of the mother was required except to avoid aortocaval compression. The anaesthetist assessed the sensory level of the block after the first hour of infusion and altered the infusion rate between 12 and 18 ml/hour as necessary. The mother was sat up to provide perineal analgesia for the second stage. A top-up of 4–8 ml bupivacaine 0.5% was given by the midwife if at any time analgesia was unsatisfactory.

Both groups were assessed by the anaesthetist 30 minutes after the initial dose of bupivacaine. The level of sensory block using an ethyl chloride spray and the degree of motor blockade using the scale described by Bromage *et al.* were recorded.¹¹ The mother was asked to score her pain using the 10-cm linear scale. Every hour following the initial assessment the midwives recorded the degree of motor block, any episodes of hypotension (systolic arterial pressure less than 80 mmHg) and whether the patient had been catheterised in the previous hour. The patient was asked to score her pain at each assessment.

The results were subjected to parametric analysis (unpaired *t*-test) and nonparametric analysis (Chi-squared test or Kolmogorov–Smirnov two-sample test) as appropriate. Statistical significance was assigned as $p < 0.05$. More important results are given with 95% confidence intervals. The Kolmogorov–Smirnov two-sample test is a nonparametric comparison of the distributions of two samples and is sensitive to differences in location, dispersion and skewness.

Results

Thirty-eight women received continuous epidural infusions and 35 intermittent tops-ups. The two groups were matched for age, weight and parity, with no significant differences (Table 1). There were seven (9%) bloody taps, five in the

Table 1. Patient data expressed as mean (SD).

	Top-up group	Infusion group
Age, years	24.8 (5.26)	25.1 (5.15)
Weight, kg	77.3 (11.61)	74.2 (7.89)
Parity, primiparous/ multiparous	23/12	30/8

infusion group and two in the top-up group. There was no significant difference between the initial doses of bupivacaine in the top-up and infusion groups, 7.4 ml (SD 0.91) and 7.4 ml (SD 1.22), respectively. There was no significant difference in the level of sensory block 30 minutes after the initial dose of bupivacaine in the two groups.

The pain scores in the two groups before the epidural was sited were not significantly different when compared using the Kolmogorov–Smirnov two-sample test, and there was

no significant difference in the pain scores 30 minutes after the epidural was sited. The quality of analgesia in the two groups throughout the remainder of labour, was compared by analysis of the best and worst hourly pain scores. This approach was used to avoid the statistical problems associated with repeated observations of the same variable. Thirty-four out of 38 patients in the infusion group compared with 25 out of 35 in the top-up group, had a best score of 1 cm or less. This difference is statistically significant (Chi squared = 4.876, d.f. = 1, $p < 0.05$) and the level of significance is consistent with a 95% confidence interval of 0.02–0.38. Sixty-four percent of all the hourly pain scores in the infusion group were 1 cm or less, compared with 53% in the top-up group. Twenty-seven patients in the infusion group compared with 15 in the top-up group, had a worst pain score of 3 cm or less. This difference is statistically significant (Chi squared = 5.928, d.f. = 1, $p < 0.025$) and the level of significance is consistent with a 95% confidence interval of 0.06 to 0.50. Thirty percent of all the hourly pain scores in the top-up group were greater than 3 cm, compared with 12% in the infusion group.

There was no significant difference in the duration of the epidural (time from insertion to delivery) in the top-up group (mean 4 hours 54 minutes, SD 2 hours 34 minutes) and the infusion group (5 hours 40 minutes SD 3 hours 27 minutes). Three patients in the top-up group required no top-ups, nine patients only one top-up, 12 patients two top-ups and 11 patients three or more top-ups. Eleven patients in the infusion group required no top-ups, 17 patients only one top-up, six patients two top-ups and four patients three or more top-ups. There was no significant difference between the total doses of bupivacaine given to the top-up group (mean 118 mg, SD 47.4) and the infusion group (135 mg, SD 59.1).

There were 12 episodes of hypotension in seven patients in the top-up group and 14 episodes of hypotension in seven patients in the infusion group. This difference is not statistically significant. Eighteen patients in the top-up group and 20 patients in the infusion group required catheterisation, which again is not statistically significant. The maximum degree of motor blockade in the two groups is shown in Table 2 and there is no statistical difference.

The mode of delivery in the two groups is shown in Table 3. There is no significant difference between the two groups when the spontaneous and instrumental delivery rates are compared using the Chi-squared test (Chi squared = 0.775, d.f. = 1, $0.04 < p < 0.30$), consistent with a 95% con-

Table 2. Maximum degree of motor blockade.

	Top-up group	Infusion group
None	13 (37%)	10 (26%)
Partial	15 (43%)	19 (50%)
Almost complete	7 (20%)	6 (16%)
Complete	0 (0%)	3 (8%)

Table 3. Mode of delivery.

	Top-up group	Infusion group
Spontaneous	18 (51%)	14 (37%)
Low forceps	4 (11%)	7 (18%)
Mid-cavity forceps	7 (20%)	5 (13%)
Ventouse	3 (9%)	5 (13%)
Caesarean section	3 (9%)	7 (19%)

fidence interval of -0.14 to $+0.36$. The duration of epidural analgesia prior to surgery in the 10 patients delivered by Caesarean section, ranged from 2 to 16 hours (mean 5 hours 55 minutes).

Discussion

The epidural administration of local anaesthetics provides good analgesia for labour. However, the sensory blockade is accompanied by motor and autonomic blockade. Motor blockade decreases the tone of the pelvic floor musculature and reduces the efficiency of active expulsive efforts by the mother. This, in the absence of an urge to push, may lead to failure of the head to rotate and descend, with prolongation of the second stage. There is an increased incidence of fetal malposition and instrumental delivery, up to 70% in primigravida patients, after epidural analgesia.^{12,13} An increased instrumental delivery rate, particularly mid-cavity forceps, represents an increased risk to the baby and mother. Autonomic blockade may result in unwanted hypotension. This decrease in arterial blood pressure may be profound and lead to fetal distress if it is accompanied by aortocaval compression.

The initial dose of bupivacaine, usually 0.25% or 0.5%, is usually followed by a repeat dose when the mother indicates that pain relief is no longer satisfactory. A concentration of 0.125% bupivacaine has been used in an effort to reduce motor and autonomic blockade but it is associated with a lower rate of satisfactory analgesia.¹⁴ There has been considerable interest in recent years in the use of epidural opioids for pain relief in labour but the results have been disappointing¹⁵; there are no demonstrable advantages over local anaesthetics and additional undesirable side effects are introduced.

The usual practice of intermittent top-ups may lead to peaks and troughs in the level of analgesia. It also makes demands upon the time of medical and midwifery staff, and there may be delays in topping up. Hypotension, which can be marked, may follow top-ups. Several authors have recommended the use of continuous epidural infusions of 0.125% or 0.25% bupivacaine at rates of 5 to 14 ml/hour, in an effort to overcome these problems.¹⁻⁹ Li *et al.*⁸ compared infusions of 0.0625% bupivacaine at a rate of 10 ml/hour with 0.125% bupivacaine at 5, 10 or 15 ml/hour. They found 0.125% bupivacaine at 10 ml/hour to be optimum. More recently, Ewen *et al.*¹⁰ compared infusions of 0.08% bupivacaine at a rate of 25 ml/hour with 0.25% bupivacaine at 8 ml/hour, and found the lower concentration to be superior.

Our study shows that a continuous epidural infusion of 0.075% bupivacaine at a rate of 12–18 ml/hour, is more effective in the provision of pain relief for labour than the standard regimen of intermittent top-ups of 0.5% bupivacaine. Peaks and troughs in the quality of analgesia were largely avoided in the infusion group. Seventy-four percent of patients in the infusion group in our study needed no or only one top-up. Top-ups were most usually needed as the mother approached full cervical dilatation or for the second stage of labour. This figure of 74% is comparable with the 69% in the optimum infusion group of Li *et al.*⁸ and 76% in the infusion group of Bogod *et al.*;⁹ both these studies used infusions of 0.125% bupivacaine. This reduction in the number of top-ups reduces the work load of the midwives

and in theory lowers the risk of acute toxicity due to inadvertent intrathecal or intravascular injection.

There was no significant difference between the total doses of bupivacaine given to the two groups in our study. Continuous infusions of 0.125% bupivacaine were compared with intermittent top-ups of 0.5% bupivacaine in an earlier study⁹ and the total dose of bupivacaine was significantly higher in the infusion group. Pharmacokinetic studies have shown that continuous epidural infusions of bupivacaine have a wide margin of safety.¹⁶ Maternal plasma concentrations of bupivacaine were no higher than with intermittent injections^{17,18} and were well below the plasma level of 1.6 µg/ml at which mild symptoms of systemic toxicity are likely to occur.¹⁹

We were unable to show any difference in the degree of motor blockade in the two groups. However, we were impressed by the lack of motor block in primigravida patients with prolonged labour; 10 patients received epidural infusions for periods of 8–16 hours. Continuous infusions of 0.125% bupivacaine may be associated with a significantly greater degree of motor blockade.⁹ The number of patients in our study is too small to make any judgment on the effect, if any, of the use of infusions on the instrumental delivery rate. Every effort was made to exclude from the study those in whom instrumental intervention was likely. Despite this, the instrumental delivery rate overall was 41%.

We recommend the use of continuous infusions of low concentration bupivacaine for all epidurals requested in primiparous patients, and in multiparous patients if in early labour.

References

1. MATOUSKOVA A, DOTTORI O, FORSSMAN L, VICTORIN L. An improved method of epidural analgesia with reduced instrumental delivery rate. *Acta Obstetrica et Gynaecologica Scandinavica* 1975; **54**: 231–5.
2. GLOVER DJ. Continuous epidural analgesia in the obstetric patient: a feasibility study using a mechanical infusion pump. *Anaesthesia* 1977; **32**: 499–503.
3. MATOUSKOVA A, HANSON B, ELMEN H. Continuous mini-infusion of bupivacaine into the epidural space during labor. Part III. A clinical study of 225 patients. *Acta Obstetrica et Gynaecologica Scandinavica* 1979; **83**(Suppl.): 43–52.
4. EVANS KRL, CARRIE LES. Continuous epidural infusion of bupivacaine in labour. A simple method. *Anaesthesia* 1979; **34**: 310–5.
5. DAVIES AO, FETTES IW. A simple safe method for continuous infusion epidural analgesia in obstetrics. *Canadian Anaesthetists' Society Journal* 1981; **28**: 484–7.
6. CLARK MJ. Continuous mini-infusion of 0.125% bupivacaine into the epidural space during labour. *Journal of the American Osteopathic Association* 1982; **81**: 484–91.
7. TAYLOR HJC. Clinical experience with continuous epidural infusion of bupivacaine at 6 ml/hr in obstetrics. *Canadian Anaesthetists' Society Journal* 1983; **30**: 277–85.
8. LI DF, REES GAD, ROSEN M. Continuous extradural infusion of 0.0625% or 0.125% bupivacaine for pain relief in primigravida labour. *British Journal of Anaesthesia* 1985; **57**: 264–70.
9. BOGOD DG, ROSEN M, REES GAD. Extradural infusion of 0.125% bupivacaine at 10 ml/hr to women in labour. *British Journal of Anaesthesia* 1987; **59**: 325–30.
10. EWEN A, MCLEOD DD, MACLEOD DM, CAMPBELL A, TUNSTALL ME. Continuous infusion epidural analgesia in obstetrics. A comparison of 0.08% and 0.25% bupivacaine. *Anaesthesia* 1986; **41**: 143–7.
11. BROMAGE PR, BURFOOT MF, CROWELL DE, PETTIGREW RT. Quality of epidural blockade. I. Influence of physical factors. *British Journal of Anaesthesia* 1964; **36**: 342–52.

12. HOULT IJ, MACLENNAN AH, CARRIE LES. Lumbar epidural analgesia in labour: relation to fetal malposition and instrumental delivery. *British Medical Journal* 1977; 1: 14-16.
13. WALTON P, REYNOLDS F. Epidural analgesia and instrumental delivery. *Anaesthesia* 1984; 39: 218-23.
14. STAINTHORP SF, BRADSHAW EG, CHALLEN PD, TOBIAS MA. 0.125% bupivacaine for obstetric analgesia? *Anaesthesia* 1978; 33: 3-9.
15. HUSEMEYER RP, O'CONNOR MC, DAVENPORT HT. Failure of epidural morphine to relieve pain in labour. *Anaesthesia* 1980; 35: 161-3.
16. DENSON DD, RAJ PP, SALDAHNA F, FINNISON RA, RITSCHEL WA, JOYCE TH, TURNER JL. Continuous perineural infusion of bupivacaine for prolonged analgesia: pharmacokinetic considerations. *International Journal of Clinical Pharmacology, Therapy and Toxicology* 1983; 21: 591-7.
17. ABBOUD TK, AFRASIABI A, SARKIS F, DAFTARIAN F, NAGAPALLA S, NOUEIHED R, KUHNERT BR, MILLER F. Continuous infusion epidural analgesia in parturients receiving bupivacaine, chloroprocaine, or lidocaine—maternal, fetal and neonatal effects. *Anesthesia and Analgesia* 1984; 63: 421-8.
18. DENSON DD, KNAPP RM, TURNER P, THOMPSON GA. Serum bupivacaine concentrations in term parturients following continuous epidural analgesia for labor and delivery. *Therapeutic Drug Monitoring* 1984; 6: 393-8.
19. REYNOLDS F, HARGROVE RL, WYMAN JB. Maternal and foetal plasma concentrations of bupivacaine after epidural block. *British Journal of Anaesthesia* 1973; 45: 1049-53.

Plasma morphine concentrations after intramuscular injection into the deltoid or gluteal muscles

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Summary

The absorption of morphine 10 mg after intramuscular injection into the gluteal and deltoid muscles was investigated. Ten patients received the injection into the deltoid and 10 were given the injection into the upper outer quadrant of the buttock. Blood was taken at frequent intervals up to 2 hours after the injection for plasma morphine analysis by high performance liquid chromatography. Morphine concentrations were generally higher in the gluteal group although the mean peak concentrations (62.8 ng/ml in the gluteal group and 52.3 ng/ml in the deltoid group) were similar. Peak morphine concentrations varied from 22.5–99.3 ng/ml in the gluteal group and 26.5–84.5 ng/ml in the deltoid group. The area under the concentration–time curve was significantly greater in the gluteal group than in the deltoid group but this difference disappeared when allowance was made for differences in body weight of the two groups. We conclude that the absorption of morphine from the deltoid and gluteal sites is similar.

Key words

*Analgesics, narcotic; morphine.
Pharmacokinetics; uptake.*

Intramuscular morphine is prescribed commonly for pre-medication and postoperative pain relief^{1,2} and is usually given by injection into the gluteal muscle. However, one study³ demonstrated erratic absorption of morphine from this route whilst a kinetic study of the absorption of morphine⁴ showed much greater consistency in both peak plasma concentration and time taken to achieve peak concentration when the injection was given into the deltoid muscle.

The aim of the present study was to compare morphine concentrations after intramuscular administration to the gluteal or deltoid muscles.

Methods

Twenty patients aged 20–66 years were studied with informed consent. All were ASA grade 1–2, scheduled to undergo elective surgery and received no regular medication. A cannula was inserted into a vein in the antecubital fossa for venous sampling. The patients were assigned randomly to receive morphine 10 mg either to the deltoid muscle or to the upper outer quadrant of the buttock. The injection was given via a 21-gauge, 1.5-inch needle by one of the investigators (T.K.). Patients in the deltoid group were given the injection in the arm contralateral to the

indwelling cannula; the needle was advanced up to the hilt into the muscle bulk at varying angles to the skin depending on the build of the patient. The needle was advanced up to the hilt perpendicular to the skin in the gluteal group.

Six millilitres of venous blood were taken for measurement of plasma morphine concentrations 0, 10, 20, 30, 45, 60, 80 and 120 minutes after the injection. The blood samples were centrifuged and the separated plasma stored at -20°C . Subsequent analysis was by high performance liquid chromatography.⁵ The patients were taken to the operating theatre for surgery at the end of the sampling period.

Statistical analysis of the data was by Student's *t*-test and the Chi-squared test. The area under the concentration–time curve (AUC) was calculated using the trapezoidal rule. Data are given as mean (SD) or mean (SEM).

Results

The age, sex, weight and height of the patients in the two groups are shown in Table 1. There was a trend towards more females in the gluteal than in the deltoid group but this was not significant. However, the patients in the deltoid group were significantly taller and heavier than the patients in the gluteal group.

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Table 1. Demographic details of patients.

	Gluteal group	Deltoid group	Significance
Age, years	43 (12)	48 (15)	NS
Sex, M:F	2:8	5:5	NS
Height, cm	162 (7)	170 (8)	$p < 0.05$
Weight, kg	62 (8)	72 (11)	$p < 0.05$

Values are mean (SD). NS, Not significant.

Table 2 shows data relating to the peak plasma concentration and the time taken to achieve peak concentration. There were no differences between the two groups.

The mean plasma concentrations of morphine at each sampling time are displayed in Fig. 1. In general, the con-

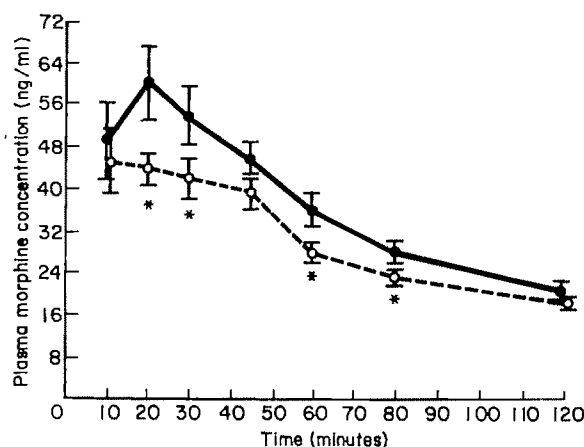


Fig. 1. Mean (SEM) plasma morphine concentrations after 10 mg intramuscular injection. ●, Deltoid group; ○, gluteal group. * $p < 0.05$.

centration of morphine was higher in the gluteal group than in the deltoid group and this reached statistical significance at 20, 30, 60 and 80 minutes after the injection.

Morphine concentrations multiplied by the weight of the patient and then averaged are plotted in Fig. 2. This transformation of the data compensates for the effect of the patient's weight on the plasma concentration of morphine. The figure shows that the weight \times concentration profile of the gluteal group is now very similar to that of the deltoid group and there are no statistically significant differences between the two groups.

Table 3 shows the mean area under the concentration–

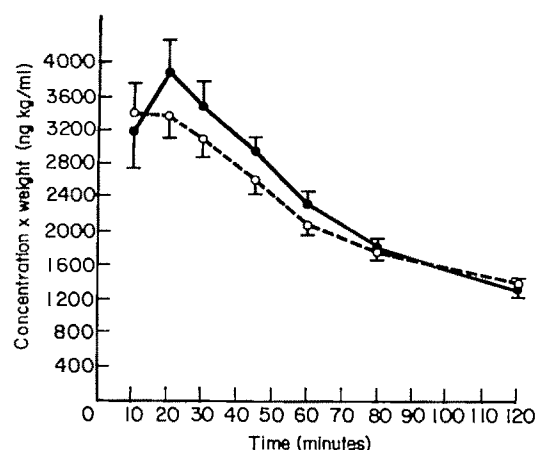


Fig. 2. Mean (SEM) weight-corrected plasma morphine concentrations. ●, Gluteal group; ○, deltoid group.

time curves. The mean AUC was significantly greater for patients in the gluteal group than for those in the deltoid group. However, the difference disappears when the data are corrected for the patients' body weight.

Discussion

The rate of absorption of morphine from the deltoid and gluteal muscles was similar since the times to achieve peak concentration did not differ significantly. There was an approximately four-fold variation in the peak plasma concentration in both groups, while the AUC varied by a factor of approximately two. This variability in the absorption of morphine after an intramuscular injection has been described by other investigators. Rigg³ found similar variability after a gluteal injection whilst Laitinen and others⁶ found a seven-fold variation in peak plasma concentration. It could be argued that this variability is due to inadvertent injection into the surrounding fat in the patients who received a gluteal injection. However, the same argument is less tenable in the deltoid group and physiological factors such as variation in muscle blood supply and vascular permeability to morphine may be important.

The plasma morphine concentration was significantly higher in the gluteal group of patients. However, this difference disappeared when allowance was made for body weight. Grabinski and colleagues⁷ compared the absorption

Table 2. Peak plasma morphine concentrations and time to peak.

	Gluteal group	Deltoid group	Significance
Mean (SEM) peak concentration, ng/ml	62.8 (7.05)	52.3 (4.9)	NS
Range of peak concentrations, ng/ml	22.5–99.3	26.5–84.5	
Mean (SEM) time to achieve peak, minutes	21.5 (2.37)	17.5 (3.73)	NS
Range of time to achieve peak, minutes	10–30	10–45	

NS, Not significant.

Table 3. Area under the concentration–time curves from 0–120 minutes.

	Gluteal group	Deltoid group	Significance
Mean (SEM) AUC, ng min/ml	4321 (350)	3473 (194)	$p < 0.05$
Range of AUC, ng min/ml	2022–5704	2397–4388	
Mean (SEM) weight-corrected data, ng min kg/ml	265832 (18164)	248221 (11272)	NS

NS, Not significant

of morphine from deltoid and gluteal sites and found significantly higher concentrations 15 minutes after injection in the deltoid group; however, her study involved cancer patients and so is not directly comparable to our study. Considerable variability in plasma concentration and a correlation between body weight and plasma concentration following intramuscular injection of diazepam were demonstrated by Gamble and colleagues.⁸

In conclusion, the absorption of morphine from the deltoid is similar to that from the gluteal muscles. Considerable variation in absorption occurs from both sites; the dosage of intramuscular morphine should be adjusted for body weight.

References

1. ADAMS AK. Psychological preparation and premedication. In: GRAY TC, NUNN JF, UTTING JE, eds. *General anaesthesia*, 4th edn. London: Butterworths, 1980: 912.
2. UTTING JE, SMITH JM. Postoperative analgesia. *Anaesthesia* 1979; **34**: 320-32.
3. RIGG JRA. Ventilatory effects and plasma concentration of morphine in man. *British Journal of Anaesthesia* 1978; **50**: 759-65.
4. STANSKI DR, GREENBLATT DJ, LOWENSTEIN MD. Kinetics of intravenous and intramuscular morphine. *Clinical Pharmacology and Therapeutics* 1978; **24**: 52-9.
5. AITKENHEAD AR, VATER M, ACHOLA K, COOPER CMS, SMITH G. Pharmacokinetics of single-dose I.V. morphine in normal volunteers and patients with end-stage renal failure. *British Journal of Anaesthesia* 1984; **56**: 813-9.
6. LAITINEN L, KANTO J, VAPAAVOURI M, VILJANEN MK. Morphine concentrations in plasma after intramuscular administration. *British Journal of Anaesthesia* 1975; **47**: 1265-7.
7. GRABINSKI PY, KAIKO RF, ROGERS AG, HOEDE RW. Plasma levels and analgesia following deltoid and gluteal injections of methadone and morphine. *Journal of Clinical Pharmacology* 1983; **23**: 48-55.
8. GAMBLE JAS, DUNDEE JW, ASSAF RAE. Plasma diazepam levels after single dose oral and intramuscular administration. *Anaesthesia* 1975; **30**: 164-9.

Transcutaneous electrical nerve stimulation after thoracotomy

Pain relief and peak expiratory flow rate—a trial of transcutaneous electrical nerve stimulation

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Summary

Forty patients scheduled to undergo thoracotomy were randomly allocated to receive either transcutaneous electrical nerve stimulation with intramuscular papaveretum (20 patients) or intramuscular papaveretum alone (20 patients) for postoperative pain relief. Total intramuscular analgesic requirements in the first 24 hours, time to satisfactory transfer to oral analgesia, antiemetic requirements and length of stay in hospital postoperatively were noted. Peak expiratory flow rate was compared pre- and postoperatively in the two groups. Use of nerve stimulation did not significantly alter the requirements for analgesia although there was a reduction in postoperative nausea and vomiting in the nerve stimulation group. There was no difference between the two groups with respect to changes in peak expiratory flow rate.

Key words

Pain; postoperative

Equipment; transcutaneous nerve stimulator.

Thoracotomy is known to cause severe postoperative pain. Both pain and narcotics interfere with respiratory function and may lead to collapse and an increased possibility of chest infection with resultant hypoxaemia. Narcotics also decrease the cough reflex and respiratory drive.

Several studies have reported that transcutaneous electrical nerve stimulation (TENS) reduces postoperative narcotic requirements, after various forms of surgery;^{1–5} more recently, however, two studies noted no difference in narcotic requirements postoperatively.^{6,7} Several of these studies^{2,5,8} showed improvements in respiratory parameters in patients who received TENS but others^{4,6} showed no difference. No difference in the incidence of nausea and vomiting between control and TENS groups was reported following thoracotomy.⁶

We report here a prospective randomised trial that assessed the effect of TENS following thoracotomy, on analgesic requirements, pain relief, peak expiratory flow rate (PEFR), requirements for antiemetic drugs and length of stay in hospital.

Methods

Forty consecutive patients scheduled to undergo thoracotomy by two consultant thoracic surgeons were studied following local ethical committee approval. Patients were allocated randomly into either TENS or control groups. All patients had pre-operative PEFR measurements with a Wright's peak flow meter, and the best of three attempts

was recorded. The patients in the TENS group had the area where the incision was to be made stimulated with a Wright Care Two-Channel Patient Kit via two test electrodes until tingling was just noted following a slow incremental increase in the intensity of stimulation. This level of stimulation was noted for postoperative use. All patients were given intramuscular papaveretum one hour pre-operatively, according to weight (<50 kg, 10 mg; 50–75 kg, 15 mg; >75 kg, 20 mg). Anaesthesia was induced with thiopentone followed by pancuronium and the trachea intubated, and anaesthesia maintained with nitrous oxide and halothane in oxygen. Fentanyl was used as an analgesic and the dose recorded. All patients had posterolateral thoracotomy incisions and the duration of the procedure was noted.

Two 9-inch electrodes were applied to either side of the thoracotomy incision at the end of the operation in the TENS group, and the stimulator connected. TENS was started before reversal of the muscle relaxant and applied continuously for 48 hours. The stimulator gave a fixed pulse rate of 70 pulses/second with a modified rectangular waveform and pulse width of 180 μ s.

All patients were given increments of papaveretum intravenously in the recovery room until they were pain free, and the total dose recorded. All patients were prescribed intramuscular papaveretum on the ward.

The nursing staff were asked to give both groups narcotic analgesia as required. Patients were visited 6, 24 and 48 hours postoperatively when pain was assessed according to

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the following scores: 0, no pain; 1, ache or discomfort; 2, pain but bearable; 3, severe pain, almost unbearable; 4, agonising pain which was the worst imaginable. The site of the major source of pain, either wound or drains, was noted since the skin incision for the drain sites did not receive stimulation in the TENS group. Patients who received TENS also had the level of stimulation checked at 6, 24 and 48 hours, to ensure that the patient was just able to appreciate a slight tingling sensation. The pain scores and level of TENS stimulation in all cases were checked by the authors only.

All patients had PEFRs checked in the morning and afternoon on the first and second postoperative days, and the best of the two readings was used for subsequent analysis. All peak flow measurements were performed and recorded by the same observer.

Patients were considered to have completed the trial satisfactorily when they were successfully established on oral analgesia, and this time was noted. The use of antiemetics was also recorded, as was the length of stay in hospital.

Statistical analysis of data was performed using Student's *t*-test in all cases except comparison of male to female numbers, which were analysed by the Chi-squared test. Fisher's exact test was applied to the data that compared sites of pain and pain scores and the use of antiemetics.

Results

Table 1 compares the two groups for age, weight, duration of operation, pre-operative, perioperative and postoperative

Table 1. Comparison of groups. Values are mean (SD).

	TENS (n = 20)	Control (n = 20)	Significance
Age, years	54 (17.8)	53 (15.7)	NS
Sex, M:F	13:7	15:5	NS
Weight, kg	61.3 (10.3)	69.2 (11.6)	p = 0.05
Duration of anaesthesia, minutes	125 (38.8)	122 (52.6)	NS
Premedication dose of papaveretum, mg	13.25 (2.45)	15.25 (2.05)	p < 0.05
Fentanyl dose perioperatively, µg	172 (71.6)	171 (42.4)	NS
Papaveretum dose in recovery, mg	7.8 (1.56)	7.7 (6.24)	NS
Papaveretum dose in first 24 hours, mg	53.5 (17.6)	52.5 (16.8)	NS
Time to oral analgesia, hours	25.7 (4.85)	26.3 (6.73)	NS
Days in hospital postoperatively	10.25 (3.82)	9.75 (2.60)	NS

NS, Not significant.

analgesic requirements, the time taken until the patients were established on oral analgesia and the duration of stay in hospital. A significant difference was found between the weights of the two groups and this is reflected in the doses of papaveretum given as premedication.

No difference between the groups was noted at 6, 24 and 48 hours in the site where pain was felt. Pain scores of 0–2 were judged to indicate satisfactory analgesia and scores of 3 or 4, unsatisfactory analgesia. No significant difference in the quality of pain relief was noted between the two groups (Table 2).

Table 2. Pain assessment 6, 24 and 48 hours postoperatively. Satisfactory:unsatisfactory pain scores.

Time postoperatively	Control (n = 20)	TENS (n = 20)
6 hours	18:2	17:3
24 hours	20:0	19:1
48 hours	19:1	20:0

Table 3. Peak expiratory flow rate comparisons. Values are mean (SD).

	TENS (n = 20)	Control (n = 20)	Significance
Percent of pre-operative predicted	77% (23.3)	84% (18.6)	NS
Percent reduction on 1st day postoperatively	38.7% (20.3)	36.4% (17.0)	NS
Percent reduction on 2nd day postoperatively	37.7% (24.0)	32.0% (19.5)	NS

The PEFRs were assessed pre-operatively as a percentage of the predicted value related to age, sex and height. Table 3 shows the pre-operative analysis; the two groups are comparable. Postoperative PEFR in the two groups as a percentage of pre-operative predicted PEFR, was compared with pre-operative PEFR as a percentage of the predicted value; no statistical difference was found between the two groups.

Five patients in the TENS group required antiemetics as opposed to 11 in the control group, which was significantly different ($p = 0.04$). No statistical difference was found between the two groups in the length of stay in hospital after operation.

Discussion

TENS is a therapeutic method for pain relief associated with minimal side effects and is based on the gate theory of pain.⁹ The level of stimulation used to produce TENS in this study, was that necessary to cause a sensation of tingling in the pre-operative test. It would not have been possible to reproduce this sensation of tingling by another means so a double-blind technique is impossible and sham TENS was not used.

Studies have been published on the use of TENS following a variety of operative procedures which have included hip surgery,¹ obstetric and gynaecological surgery,² abdominal surgery^{3,4} and hip, lumbar spine and gynaecological laparotomies in the same study.⁵ All found that TENS reduced the amount of narcotic agent required. One study³ found an improvement in pulmonary function in the TENS groups, although obese patients, smokers and those with respiratory symptoms were specifically excluded and hence the findings on pulmonary function cannot be applied to post-thoracotomy patients. Early ambulation and absence of respiratory complications have also been noted.² Three studies of a mixed group of patients included thoracotomies.^{8,10,11} A reduction in atelectasis with TENS was reported in one study⁸ but the control group was a retrospective comparison. Reduced narcotic requirements have been reported to follow TENS in a small number of thoracotomy patients.^{10,11}

Forced vital capacity was shown to improve during the

following 10-minute bursts of TENS on the second postoperative day following thoracotomy, although this study included any incision in the chest wall.¹² Rooney *et al.*¹³ studied 22 cases in both control and TENS groups and found that five cases in the TENS group required no narcotic analgesia in the first 24 hours after thoracotomy but all 22 cases required analgesia in the control group, a highly significant difference. Warfield and her colleagues⁶ found no difference in the amount of narcotic administered but significantly lower pain scores in the TENS group. They also noted a significantly shorter postoperative stay in the intensive care unit. More recently, a large prospective study following abdominal surgery⁷ found no difference in morphine requirements or postoperative pain scores between TENS and sham therapy groups. These workers also showed no difference in either arterial oxygen tensions or the incidence of postoperative pulmonary complications in the two groups.

We tried in our study to determine whether TENS is beneficial in terms of pain relief and improvement in pulmonary function. We were unable to show any improvement in patient comfort with TENS; also, application of TENS to the wound but not the drain site, did not decrease the frequency of pain experienced from the wound site. No alteration in PEFR was shown either on the first or second postoperative day in the two groups.

We were unable to show any difference in length of stay in hospital between the two groups in spite of previous reports of early ambulation with TENS,² and a shorter stay in the intensive care unit.⁶ There was, however, a significant reduction in the number of patients who required antiemetics in the TENS group. There have been conflicting reports in the past concerning nausea⁶ and ileus^{4,14,15} and whether TENS has a direct effect on the gastrointestinal tract or acts via the autonomic nervous system. We conclude that TENS produces no benefits in terms of pain relief after thoracotomy.

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References

1. PIKE PNH. Transcutaneous electrical stimulation. Its use in the management of postoperative pain. *Anaesthesia* 1978; 33: 165-71.
2. EVRON S, SCHENKER JG, OLSHWANG D, GRANAT M, MAGORA F. Postoperative analgesia by percutaneous electrical stimulation in gynecology and obstetrics. *European Journal of Obstetrics, Gynaecology and Reproductive Biology* 1981; 12: 305-13.
3. ALI J, YAFFE CS, SERRETTE C. The effect of transcutaneous electrical nerve stimulation on postoperative pain and pulmonary function. *Surgery* 1981; 89: 507-12.
4. COOPERMAN AM, HALL B, MIKALACKI K, HARDY R, SADER E. Use of transcutaneous electrical stimulation in the control of postoperative pain. Results of a prospective, randomized, controlled study. *American Journal of Surgery* 1977; 133: 185-7.
5. SOLOMAN RA, VIERNSTEIN M, LONG DM. Reduction of postoperative pain and narcotic use by transcutaneous electrical nerve stimulation. *Surgery* 1980; 87: 142-6.
6. WARFIELD CA, SKEIN JM, FRANK HA. The effect of transcutaneous nerve stimulation on pain after thoracotomy. *Annals of Thoracic Surgery* 1985; 39: 462-5.
7. CUSCHIERI RJ, MORRAN CG, MCARDLE CS. Transcutaneous electrical stimulation for postoperative pain. *Annals of the Royal College of Surgeons of England* 1985; 67: 127-9.
8. HYMES AC, RAAB DE, YONEHIRO EG, NELSON DG, PRINTY AL. Electrical surface stimulation for control of acute postoperative pain and prevention of ileus. *Surgical Forum* 1973; 24: 447-9.
9. MELZACK R, WALL PD. Pain mechanisms: a new theory. *Science* 1965; 150: 971-9.
10. VAN DERARK GD, McGRATH KA. Transcutaneous electrical stimulation in treatment of postoperative pain. *American Journal of Surgery* 1975; 130: 338-40.
11. NEARY JM. Transcutaneous electrical nerve stimulation for the relief of post-incisional surgical pain. *American Association of Nurse Anaesthetists Journal* 1981; 49: 151-5.
12. STRATTON SA, SMITH MM. Postoperative thoracotomy. Effect of transcutaneous electrical nerve stimulation on vital capacity. *Physical Therapy* 1980; 60: 45-7.
13. ROONEY SM, JAIN S, GOLDINER PL. Effect of transcutaneous nerve stimulation on postoperative pain after thoracotomy. *Anesthesia and Analgesia* 1983; 62: 1010-2.
14. HYMES AC, YONEHIRO EF, RAAB DE, NELSON GD, PRINTY AL. Electrical surface stimulation for treatment and prevention of ileus and atelectasis. *Surgical Forum* 1974; 25: 222-4.
15. ROSENBERG M, CURTIS L, BOURKE DL. Transcutaneous electrical nerve stimulation for the relief of postoperative pain. *Pain* 1978; 5: 129-33.

CASE REPORT

Acetylcholinesterase – a specific marker for cerebrospinal fluid

R. G. VANNER

Summary

An oedematous pre-eclamptic patient received lumbar epidural analgesia during labour. Clear fluid leaked from the skin puncture site for 4 days. The fluid was analysed using protein electrophoresis for cholinesterase enzymes and was found not to contain the cerebrospinal fluid specific form of the enzyme, acetylcholinesterase. The sensitivity of this test was explored using serial dilutions of cerebrospinal fluid. It is now possible to say that the leaking fluid did not contain cerebrospinal fluid.

Key words

Complications; oedema, dural puncture.

Enzymes; acetylcholinesterase.

Two groups recently reported difficulty in the differentiation between interstitial fluid and cerebrospinal fluid (CSF) after an epidural catheter was inserted through oedematous tissue.^{1,2} In both cases protein concentration was used as identifier because interstitial fluid contains 3–20 g/litre of protein whereas CSF has only 0.2–0.4 g/litre. However, a fistula between the subarachnoid space and the skin would be missed if interstitial fluid is diluted by CSF. A continuing fistula could be a serious infection risk.

This is a report of a similar case and I proposed that the fluid be analysed qualitatively using protein electrophoresis for CSF specific acetylcholinesterase in addition to the more usual quantitative estimation of total protein. CSF contains nonspecific cholinesterases and a soluble acetylcholinesterase isoenzyme which passes across the ependyma from central cholinergic neurones.³ Other body fluids have nonspecific cholinesterase synthesised in the liver but contain only small amounts of acetylcholinesterase. Serum may also contain acetylcholinesterase from red blood cells if the sample has been haemolysed. CSF may be differentiated from other body fluids by protein electrophoresis to show the neural specific isoenzyme.

Case history

A 26-year-old primigravida at term with pre-eclampsia had gross dependent oedema up to mid-abdomen with a gain in weight from 68.5 to 80 kg in the last 23 weeks of her pregnancy. Labour was induced with prostaglandin pessaries; the first stage lasted 10 hours and the second stage 1 hour 25 minutes, with delivery aided by Keilland's forceps of a live female who weighed 3.5 kg.

A lumbar epidural was performed at L_{3/4} 2 hours after the start of labour. A puncture was made with a 15-scalpel blade after skin preparation. Considerable pitting oedema was massaged away and the epidural space identified at 5 cm using a 16-gauge Tuohy needle; 3 cm of catheter was left in the space. There was no suggestion at this stage that the dura was punctured. Her pain relief was managed with four doses of 10 ml 0.25% bupivacaine. The sensory level was at T₁₀ and she retained motor function of her legs throughout.

It was noticed 2 hours after insertion of the epidural catheter that the dressing and bed linen were wet; clear fluid was leaking around the epidural catheter. No fluid could be aspirated through the catheter. Further top-ups were given cautiously by an anaesthetist, in case the dura was punctured. The catheter was removed 12 hours after insertion but the fluid continued to leak for a further 4 days and she needed frequent changes of the sterile dressing. It was difficult to estimate exactly how much fluid leaked but her bed linen was saturated after the first night.

Method

The presence of the two enzymes is demonstrated by a white precipitate of copper thiocholine after protein electrophoresis of the fluid on polyacrylamide gel and incubation with acetylthiocholine in the presence of copper ions. Normal CSF exhibits a fast moving acetylcholinesterase band and a slower moving nonspecific cholinesterase band. This test is used in the routine investigation of amniotic fluid obtained by amniocentesis from mothers at high risk of producing infants with neural tube defects,⁴ since the

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neural specific isoenzyme appears in the amniotic fluid when an open neural tube defect is present.

Results

The protein concentration of the fluid by reagent strips (Ames Albustix) was over 3 g/litre. (It should be noted that chlorhexidine antiseptic solutions give a false positive with these sticks.) The later laboratory estimation was 7.1 g/litre. The fluid was therefore unlikely to be CSF alone but the possibility that it was a mixture of CSF and interstitial fluid could not be excluded.

Examination of the fluid by protein electrophoresis showed a nonspecific cholinesterase band but did not show an acetylcholinesterase band. The sensitivity of this method was tested by electrophoresis of serial dilutions of CSF (Fig. 1). Concentrations of CSF greater than one part in 20 can

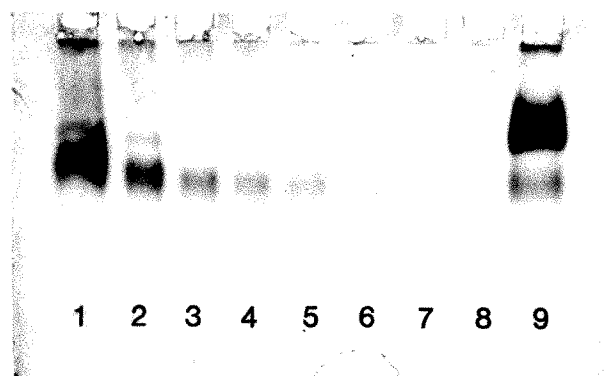


Fig. 1. Protein electrophoresis of serial dilutions of CSF. 1, Neat; 2, 1 in 2; 3, 1 in 4; 4, 1 in 6; 5, 1 in 8; 6, 1 in 10; 7, 1 in 20; 8, 1 in 40; 9, amniotic fluid from a fetus with a neural tube defect. The lower band is acetylcholinesterase, the other is nonspecific cholinesterase.

be identified. The fluid therefore contained less than one part in 20 CSF and was therefore unlikely to be from a fistula between the subarachnoid space and the skin.

Discussion

Cerebrospinal fluid can be differentiated from other body fluids by the estimation of protein content both at the bedside with reagent strips and by later confirmation in the laboratory. In some clinical situations, such as the case described and with fluid leakage from the nose or ear, a more specific noninvasive test is needed for the identification of CSF which may take longer to perform. The immunochemical identification of a second band of transferrin has been described⁵ after the protein electrophoresis of CSF, but this test is not readily available. Protein electrophoresis for acetylcholinesterase can be used to identify CSF and is positive even after a one in 20 dilution. Less than 0.5 ml is required and our regional neural tube defect screening laboratory was pleased to include our sample amongst their weekly batch of amniotic fluid samples.

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References

1. KIRBY IJ, RYAN TDR. Generalised oedema and epidural anaesthesia. *Anaesthesia* 1985; **40**: 709-10.
2. DOWNEY L, SLATER EM, ZEITLIN GL. Differentiating interstitial fluid from cerebral spinal fluid. *Anesthesiology* 1985; **63**: 120.
3. CHUBB IW, GOODMAN S, SMITH AD. Is acetylcholinesterase secreted from central neurons into the cerebrospinal fluid? *Neuroscience* 1976; **1**: 57-62.
4. WALD NJ, CUCKLE HS. Amniotic fluid acetylcholinesterase electrophoresis as a secondary test in the diagnosis of an encephaly and open spina bifida in early pregnancy. Report of the Collaborative Acetylcholinesterase Study. *Lancet* 1981; **2**: 321-4.
5. MEURMAN OH, IRJALA K, SUONPAA J, LAURENT B. A new method for the identification of cerebrospinal fluid leakage. *Acta Otolaryngologica* 1979; **87**: 366-9.

CASE REPORT

Adriamycin cardiomyopathy

Fatal outcome of general anaesthesia in a child with Adriamycin cardiomyopathy

P. J. McQUILLAN, B. A. MORGAN AND J. RAMWELL

Summary

The death under general anaesthesia of a child with Adriamycin cardiomyopathy is reported. The acute, subacute and chronic cardiotoxic effects of Adriamycin are discussed and the risk factors for chronic Adriamycin cardiomyopathy presented, with particular reference to cumulative dosage of Adriamycin. The insidious onset of impairment of cardiac function is stressed and suggestions for anaesthetic management outlined.

Key words

Heart; cardiomyopathy.
Cytotoxics; Adriamycin.

The treatment of malignant disease with cytotoxic drugs has implications for anaesthesia^{1,2} because the side effects include dysfunction of a variety of organs of relevance to anaesthetic management. Identification of the components of combination chemotherapy is therefore crucial to the safe management of these patients.

A number of cytotoxic agents are cardiotoxic, notably the anthracycline antibiotics, doxorubicin (Adriamycin) and daunorubicin. Postoperative death has been reported in patients treated with Adriamycin but we believe that this report is the first of intra-operative death in an anaesthetised child with Adriamycin cardiomyopathy.

Case history

A 9-year-old girl presented for anaesthesia for emergency insertion of a central venous catheter to facilitate parenteral antibiotic and fluid therapy. At 5 years of age a rhabdomyosarcoma of the lower lip had been excised and initial chemotherapy consisted of Adriamycin, cyclophosphamide and vincristine for one year. There was a local recurrence 3 years later but surgical clearance was impossible. At this stage, following a cumulative dose of 480 mg/sq m Adriamycin, a single echocardiogram suggested that normal ventricular function was present and it was felt justified to treat the recurrent disease with an Adriamycin-based regimen (Adriamycin, vincristine, cyclophosphamide and later Adriamycin, vincristine, etoposide and cisplatin).

There were multiple hospital admissions over the next 12 months because of thrombocytopenia, leucopenia and

repeated infections. The acute onset of high fever, malaise, diarrhoea and vomiting following a 6-week history of dry cough, precipitated a further admission.

Venous access had become a major problem and she required general anaesthesia to establish a peripheral infusion for parenteral antibiotics. An inhalational induction with nitrous oxide, oxygen and enflurane was accomplished despite persistent coughing. The peri-operative period was otherwise uneventful. The peripheral infusion was short-lived and 48 hours later she presented for emergency insertion of a long-term central venous catheter.

The patient was unwell on examination; she had a dry cough and was severely dehydrated as a result of diarrhoea and vomiting. She had a low volume regular pulse of 120 beats/minute. Arterial blood pressure was 85/40 mmHg, heart sounds were normal, jugular venous pressure was not elevated, there was no oedema and the liver was tender but not enlarged. There were scattered inspiratory crepitations at the right base only. She was apyrexial.

Laboratory investigations revealed a haemoglobin concentration of 133 g/litre, sodium 114 mmol/litre, potassium 2.7 mmol/litre, chloride 84 mmol/litre, urea 18.4 mmol/litre, creatinine 185 µmol/litre, total calcium 2.12 mmol/litre and magnesium 0.74 mmol/litre. Electrocardiography (ECG) showed sinus rhythm with T-wave inversion in the anterior chest leads. A chest radiograph was reported to be normal.

The anaesthetist was unable to establish the precise cumulative dosage of Adriamycin. Later enquiry revealed

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the total dose to be 880 mg/sq m; in addition, she had received cyclophosphamide 10 000 mg/sq m and cisplatin 170 mg/sq m.

No premedication was prescribed. Anaesthesia was induced with nitrous oxide, oxygen and halothane after ECG monitoring had been established. Induction was difficult since it was prolonged and complicated by persistent coughing. A forearm vein was cannulated after induction had been completed. The patient became severely hypotensive shortly after this, however, with the development of atrial fibrillation followed rapidly by cardiac arrest in ventricular fibrillation. Prolonged resuscitation was unsuccessful.

Postmortem examination revealed bilateral pleural effusions, oedematous lungs, congestion of the liver and some ascites. There was a pericardial effusion of 40 ml and a dilated, mildly hypertrophied left ventricle. On microscopy there was some interstitial fibrosis, variation in fibre size, and some swollen, distorted mitochondria. There was no evidence of myocarditis. A consultant pathologist considered that these cardiomyopathic changes were due to Adriamycin.

Discussion

The combination of several factors in this patient culminated in ventricular fibrillation. These included marked dehydration, hypovolaemia and impaired renal function due to vomiting and diarrhoea; severe electrolyte disturbance that included gross hypokalaemia and hyponatraemia; deep halothane anaesthesia; an underlying Adriamycin-induced congestive cardiomyopathy; and an emergency anaesthetic procedure.

There was no satisfactory means to improve the pre-operative condition of the patient. It seems unlikely that resuscitation by rectal or subcutaneous infusions would have been effective in the face of continuing fluid loss due to diarrhoea and vomiting. The choice of halothane was made in the expectation of a reliable induction in an uncooperative child with inaccessible veins, bearing in mind the difficulties encountered on the previous occasion using enflurane.

There appears, despite the paucity of clinical signs, to have been an underlying congestive cardiomyopathy which followed a very high cumulative dosage of Adriamycin, perhaps compounded by other potentially cardiotoxic agents. The T-wave inversion in the anterior chest leads of the ECG provided an indication of a cardiac abnormality although these changes have not been noted previously in cardiomyopathy associated with Adriamycin. The single echocardiographic study 12 months earlier failed to demonstrate any abnormality after a cumulative dose of 480 mg/sq m Adriamycin. Serial or exercise echocardiography (*vide infra*) following further Adriamycin administration might have documented the deterioration of ventricular function at an earlier stage.

Ventricular fibrillation was reported during intravenous infusion of the antiemetic domperidone³ but none was prescribed during the patient's final illness.

Doxorubicin hydrochloride (Adriamycin) is an anthracycline antibiotic used extensively in chemotherapy for malignant disease, including many tumours in children. In Newcastle 6500 operations were performed on children

under 16 years of age in 1985 and 3% of these involved children with cancer which had been treated with Adriamycin.

Cytotoxicity and side effects

The cytotoxic action of Adriamycin occurs by intercalation with DNA bases which partly uncoils the helical structure and thus inhibits the template function of DNA and inhibits DNA polymerase.^{4,5} Therefore side effects are seen in rapidly dividing tissues, and include myelosuppression, stomatitis, gastro-intestinal disturbance, alopecia and occasionally hepatic damage.^{5,6}

Cardiotoxicity

The major factor that limits the use of Adriamycin is cardiotoxicity. Several types have been described.

Acute non-specific ECG changes.^{4,7,8} Reversible and self-limiting nonspecific ECG changes may occur in 10–25% of patients. These changes are not dose related, appear during or shortly after Adriamycin administration and resolve over 1–2 weeks. Elevated levels of histamine and catecholamines may be partly responsible for these changes which include ST depression, T-wave flattening, prolongation of the QT interval, ventricular or supraventricular dysrhythmias and heart block.

Subacute cardiotoxicity.^{4,7,9} A toxic cardiopathy has been described in young, fit patients related to a pericarditis and/or myocarditis in which cardiac dysfunction may develop within 4 weeks of Adriamycin administration. In addition more acute Adriamycin-induced myocardial damage may occur, particularly in elderly patients or those with pre-existing cardiac disease. Cardiac failure and myocardial infarction have occurred shortly after initiation of Adriamycin treatment.

Chronic cardiotoxicity. The risk factors in chronic cardiotoxicity are well defined.^{4,10,11} Adriamycin cardiomyopathy is dose related. One percent of patients develop cardiomyopathy at cumulative doses of less than 500 mg/sq m and the incidence increases to 11% at doses of 500–600 mg/sq m and 30% following more than 600 mg/sq m. Mediastinal irradiation is the next most important determinant of cardiotoxicity.^{4,12}

Synergistic cardiotoxicity is also said to occur with other cytotoxic agents, particularly cyclophosphamide, mitomycin C, actinomycin D, mithramycin, vincristine and bleomycin.^{4,11,12} Cardiotoxicity due to cisplatin has been reported but is rare.¹³ Adriamycin cardiotoxicity is seen at lower doses in patients with pre-existing heart disease or hypertension.¹⁰ The elderly and the very young appear to be more susceptible than young adults.^{4,10} The schedule of administration is important since cardiotoxicity is greater using a 3-weekly cycle than a weekly regimen.^{4,11,14} Beta blockers and calcium antagonists exacerbate myocardial dysfunction in patients treated with Adriamycin.²

The congestive cardiomyopathy induced by Adriamycin is indistinguishable clinically from that due to other causes. Anthracycline damage is considered by some authorities to be characteristically defined in serial endomyocardial biopsies. However, findings at postmortem are usually nonspecific.^{15,16}

Mechanism of cardiotoxicity

The mechanism of cardiotoxicity is thought to be related to superoxide free-radical production.^{4,7} The susceptibility of the heart is probably related to its relative deficiency in superoxide dismutase and a poor hexose monophosphate (HMP) shunt, which is required to generate NADPH for electron transfer in the detoxification of superoxide. Adriamycin also depletes the enzyme glutathione peroxidase, which is responsible normally for the metabolism of hydrogen peroxide. Mitochondrial damage may also occur by lipid peroxidation of mitochondrial membranes, depletion of mitochondrial proteins or inhibition of co-enzyme Q₁₀, a key enzyme in oxidative phosphorylation.⁴

Prevention of cardiotoxicity

Prevention of cardiotoxicity centres on limitation of Adriamycin dosage.⁴ Free-radical scavengers (vitamin E, acetylcysteine), co-enzyme Q₁₀, carnitine, adenosine, a chelating agent derived from EDTA and digoxin have not proved effective in the limitation of cardiotoxicity. Current research involves Adriamycin derivatives with low cardiotoxic potential, such as epirubicin and idarubicin, and linking of Adriamycin to tumour-specific antibodies or macromolecules.¹⁷

Identification of cardiotoxicity

Identification of Adriamycin-induced ventricular impairment may not be easy. Clinical and radiological evidence of cardiomegaly and heart failure is known to appear at a relatively late stage. ECG changes may be seen (low voltage, loss of P-wave amplitude and clockwise rotation) but these are nonspecific.⁴ Direct morphological assessment by endomyocardial biopsy and electron microscopy¹⁸ is possible but invasive, and difficult in children. Systolic time intervals^{19,20} have been used but are unreliable. Two-dimensional M-mode echocardiography and radionuclide scintigraphy are widely employed techniques;^{18,21,22} serial and exercise testing are more discriminating than single tests at rest.²³

Anaesthetic assessment

Careful history and clinical examination are important, in view of the insidious onset of ventricular dysfunction. Information about all cytotoxic agents used, and particularly the exact cumulative doses of Adriamycin, must be available. Smith and DasGupta⁶ recommend that patients who receive more than 250 mg/sq m Adriamycin, or 150 mg/sq m with mediastinal irradiation, should undergo cardiological assessment that includes ECG, chest radiography and echocardiography. Jonsson,²⁴ however, preferred radionuclide scintigraphy. Follow-up is recommended with subsequent increments of 50–100 mg/sq m Adriamycin.

Peri-operative problems

Peri-operative problems in patients treated with Adriamycin include intra-operative hypotension and dysrhythmias⁸ and postoperative heart failure.^{8,24} Smith and DasGupta⁶ described late pulmonary oedema and death within 24

hours of surgery when intra-operative Adriamycin was administered.

Anaesthetic technique

Classical teaching is to maintain a stable haemodynamic state in the peri-operative period. Pre-operative abnormalities such as hypoxia, hypovolaemia and electrolyte disturbance should be corrected as far as possible. Patient anxiety may be minimised with 'heavy' premedication using a benzodiazepine or papaveratum and hyoscine. Local or regional anaesthesia could be considered although there are few published reports of its use in these patients;^{6,11} these techniques alone are generally tolerated poorly by children. Agents with adverse cardiovascular effects should be avoided. Etomidate is the induction agent of choice in combination with an opioid such as fentanyl, and positive pressure ventilation after vecuronium or atracurium. The inhalational agents are best avoided or used in low concentrations; isoflurane is the least cardiodepressant. Cardiovascular monitoring must begin before induction; ECG and indirect blood pressure measurements are minimal requirements, and pulse oximetry and capnography are recommended; direct arterial and central venous or pulmonary arterial catheters are used in patients with more severely impaired ventricular performances. Monitoring into the postoperative period will identify patients who develop late heart failure. Peri-operative Adriamycin administration should be avoided in view of the potential for dysrhythmias and acute deterioration in ventricular function.²⁴

The authors faced with a similar problem again, would consider intramuscular ketamine or an inhalational induction with isoflurane, although we do not believe that the outcome would be changed.

Conclusions

The cardiomyopathy associated with the use of Adriamycin is insidious in onset and anaesthesia in its presence may be a life-threatening event. It is important to determine the cumulative dosage of Adriamycin and other potentially cardiotoxic agents. Patients in high risk groups or those with clinical evidence of myocardial impairment should be referred for cardiological assessment with ECG, chest radiography and echocardiography or radionuclide scintigraphy. Anaesthesia should be carried out by an experienced anaesthetist and vital parameters should be monitored closely.

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References

1. SELVIN BL. Cancer chemotherapy: Implications for the anesthesiologist. *Anesthesia and Analgesia* 1981; **60**: 425–34.
2. CHUNG F. Cancer chemotherapy and anaesthesia. *Canadian Anaesthetists' Society Journal* 1982; **29**: 364–71.
3. BOUSSAK JB, CAREY P, PARRY H. Cardiac arrest after treatment with intravenous domperidone. *British Medical Journal* 1984; **289**: 1579.

4. UNVERFERTH DV, MAGORIEN RD, LEIER CV, BALCERZAK SP. Doxorubicin cardiotoxicity. *Cancer Treatment Reviews* 1982; **9**: 149-64.
5. CALABRESI P, PARKS RE. Chemotherapy of neoplastic diseases. In: GILMAN AG, GOODMAN LS, GILMAN A, eds. *The pharmacological basis of therapeutics*, 6th edn. New York: Macmillan, 1980: 1249-313.
6. SMITH RM, DASGUPTA V. Adriamycin cardiotoxicity. *Anesthesiology Review* 1981; **8**: 14-19.
7. WOODHOUSE KW, BLAIN PG. Some organ-specific adverse reactions to cytotoxic drugs. *Adverse Drug Reactions and Acute Poisoning Reviews* 1983; **2**: 123-43.
8. BURROWS FA, HICKEY PR. Perioperative complications in patients with anthracycline chemotherapeutic agents. *Canadian Anaesthetists' Society Journal* 1985; **32**: 149-57.
9. BRISTOW MR, THOMPSON PD, MARTIN RP, MASON JW, BILLINGHAM ME, HARRISON DC. Early anthracycline cardiotoxicity. *American Journal of Medicine* 1978; **65**: 823-32.
10. VON HOFF DD, LAYARD MW, BASA P, DAVIS HL, VON HOFF AL, ROZENCWEIG M, MUGGIA FM. Risk factors for doxorubicin-induced congestive heart failure. *Annals of Internal Medicine* 1979; **91**: 710-17.
11. CAVIALE P, MCCLELLAN EL. Adriamycin toxicity. Effects in subsequent anesthesia and surgery. *Journal of the Kansas Medical Society* 1981; **82**: 553, 574.
12. PRAGA C, BERETTA G, VIGO PL, LENAZ GR, POLLINI C, BONADONNA G, CANETTA R, CASTELLANI R, VILLA E, GALLAGHER CG, VON MELCHNER H, HAYAT M, RIBAUD P, DE WASCH G, MATTSOON W, HEINZ R, WALDNER R, KOLARIC K, BUEHNER R, BOKKEL-HUYNINCK WT, PEREVODCHIKOVA NI, MANZIUK LA, SENN HJ, MAYR AC. Adriamycin cardiotoxicity: a survey of 1273 patients. *Cancer Treatment Reports* 1979; **63**: 827-34.
13. WILTSHAW E, CARR B. *cis*-Cisplatinum(II) diaminodichloride. Clinical experience of the Royal Marsden Hospital and Institute of Cancer Research. *Recent Results in Cancer Research* 1974; **48**: 178-82.
14. TORTI FM, BRISTOW MR, HOWES AE, ASTON D, SROCKDALE FE, CARTER SK, KOHLER M, BROWN BW, BILLINGHAM ME. Reduced cardiotoxicity of doxorubicin delivered on a weekly schedule. Assessment by endomyocardial biopsy. *Annals of Internal Medicine* 1983; **99**: 745-9.
15. FERRANS VJ. Morphologic assessment of cardiac lesions caused by anthracyclines. In: MUGGIA FM, YOUNG CW, CARTER SK, eds. *Anthracycline antibiotics in cancer therapy*, Vol. 10. The Hague: Martinus Nijhoff, 1982: 331-47.
16. BILLINGHAM ME. Some recent advances in cardiac pathology. *Human Pathology* 1979; **10**: 376-86.
17. MERZ B, HAGER T. Defusing adverse effects of anticancer drugs. *Journal of the American Medical Association* 1983; **250**: 459.
18. BRISTOW MR. Cardiac monitoring of patients receiving anthracyclines. In: MUGGIA FM, YOUNG CW, CARTER SK, eds. *Anthracycline antibiotics in cancer treatment*, Vol. 10. The Hague: Martinus Nijhoff, 1982: 348-51.
19. BALCERZAK SP, CHRISTAKIS J, LEWIS RP, OLSEN HM, MALSPEIS L. Systolic time intervals in monitoring adriamycin-induced cardiotoxicity. *Cancer Treatment Reports* 1978; **62**: 893-9.
20. RINEHART JJ, LEWIS RP, BALCERZAK SP. Adriamycin cardiotoxicity in man. *Annals of Internal Medicine* 1974; **81**: 475-8.
21. SINGER JW, NARAHARA KA, RITCHIE JL, HAMILTON GW, KENNEDY JW. Time- and dose-dependent changes in ejection fraction determined by radionuclide angiography after anthracycline therapy. *Cancer Treatment Reports* 1978; **62**: 945-8.
22. GOTTDIENER JS. Noninvasive assessment of cardiac dysfunction in the cancer patient. *Cancer Treatment Reports* 1978; **62**: 949-53.
23. GOTTDIENER JS, MATHISEN DJ, BORER JS, BONOW RO, MYERS CE, BARR LH, SCHWARTZ DE, BACHARACH SL, GREEN MV, ROSENBERG SA. Doxorubicin cardiotoxicity: assessment of late left ventricular dysfunction by radionuclide cineangiography. *Annals of Internal Medicine* 1981; **94**: 430-5.
24. JONSSON T, MORTENSEN SA, AABO K. Acute cardiac failure precipitated by anesthesia and surgery in patients treated with adriamycin. *Ugeskrift for Laeger* 1984; **146**: 3837-9.

CASE REPORT

Ischaemic pain in Buerger's disease

Report of a female patient receiving long-term local analgesia

J. M. SADDLER AND M. M. CROSSE

Summary

A female patient with Buerger's disease developed severe ischaemic pain in her left index finger which was refractory to several therapeutic measures. A silastic catheter inserted in the region of the median nerve at the elbow was topped up intermittently with local anaesthetic for 6 weeks and effected excellent analgesia. The catheter was removed when the pain had abated, and the finger tip later amputated.

Key words

Anaesthetic techniques, regional; median nerve block.

Complications; gangrene, Buerger's disease.

Buerger's disease (thromboangiitis obliterans) is a condition that occurs in cigarette smokers and is characterised by peripheral arterial and venous occlusions. We present here a case where ischaemic pain unrelieved by other therapies was alleviated by median nerve block which was maintained for 6 weeks so as to allow delayed surgical intervention.

Case history

A 37-year-old white female was admitted with severe pain after minor trauma to the tip of her left index finger. Buerger's disease had been diagnosed 10 years previously and there was histological and radiological confirmation of the condition. She had undergone several operations to alleviate the complications of the disease; these included bilateral lumbar sympathectomy, a through-knee amputation of the right leg, a right cervical sympathectomy and an amputation of her right index finger. She had been treated with spinal cord stimulation and had received a thoracic epidural with phenol in glycerine in addition to these procedures, in an attempt to mitigate the ischaemic pain in her leg and fingers, respectively. She had been a heavy smoker in the past and had reduced, but not eliminated, her tobacco consumption.

On examination she had a red, swollen and exquisitely painful left index finger. No peripheral pulses were detectable in the arms distal to the brachial arteries, which were barely palpable. Initial therapy included elevation of the left hand, intravenous naftidrofuryl (Praxilene) and intramuscular pethidine. A left cervical sympathectomy was carried out and the patient was discharged shortly afterwards;

oral methadone was given for analgesia. She was readmitted 2 weeks later with worsening pain in the finger, which had now developed dry gangrene.

The limb was again elevated and intravenous naftidrofuryl restarted. Large doses of methadone, papaveretum and buprenorphine failed to give adequate pain relief and the patient was transferred to the neurological centre where cervical epidural electrodes were inserted and spinal cord stimulation commenced. This achieved partial relief but unfortunately the beneficial effect was short lived. A left subclavian arteriogram demonstrated severe arterial occlusions distal to the elbow; the forearm and hand were supplied almost solely by a tortuous interosseus artery (Fig. 1).

It was thought, because of this critical circulation, that an amputation of the finger tip would result in poor wound healing and eventually a major proximal amputation. This



Fig. 1. Left subclavian arteriogram.

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would greatly incapacitate the patient since she required crutches to walk.

An anaesthetist's opinion was sought at this stage on the management of the ischaemic pain. Initially a brachial plexus block was carried out by the axillary approach using an epidural catheter introduced via a Tuohy needle. This achieved complete pain relief but the motor block prevented the patient from using her crutches. The brachial plexus block was replaced by median nerve block, in order to retain the patient's mobility. This had to be done above the level of the elbow since it was felt that trauma below this point might lead to further gangrene.

The introducer from a silastic feeding catheter pack (Vygon Nutricath 16 gauge) was inserted percutaneously under sterile conditions, just medial to the aponeurosis of the biceps tendon and a faintly palpable brachial artery, at the level of a line drawn between the two epicondyles.¹ Two millilitres 1% plain lignocaine were injected at a depth of 1 cm through the introducer and gave immediate pain relief. A further 15 ml lignocaine were injected and the silastic feeding catheter introduced into the space produced by this large volume. The introducer was withdrawn and the catheter sewn in position. A sterile dressing was applied and a bacterial filter attached (Fig. 2). It was found that

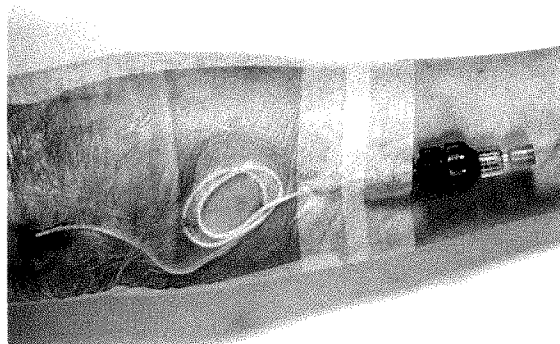


Fig. 2. Left forearm with Nutricath sewn in position covered by clear dressings.

15 ml 0.5% plain bupivacaine provided over 20 hours of analgesia, and that while sensation was returning adequate analgesia could be achieved with oral Distalgesc. She was therefore discharged home and her general practitioner agreed to arrange for local anaesthetic top-ups every 24 hours.

The catheter had been in position for 6 weeks when she noticed that the pain did not return at the end of the 24-hour period. A top-up was omitted and the finger was found to have become free of pain. The catheter was therefore removed. There was no evidence of infection. The finger tip was later removed with minimal surgical intervention and good healing took place. The patient remains reasonably well although she has recently undergone a Gritti-Stokes amputation of the left leg.

Discussion

The original description of thromboangiitis obliterans was made by von Winiwarter in 1879² but the disease is attri-

buted to Buerger who described it more fully in 1908.³ The condition is characterised by peripheral arterial and venous occlusion. Women are believed to constitute less than 1% of all patients with this rare disease,⁴ although recently there seems to have been a relative increase in incidence which may be related to their increased use of tobacco.⁵ As in males the condition is associated strongly with cigarette smoking⁶ and usually abates if smoking is discontinued.⁷ All four limbs are commonly affected but, unlike atherosclerosis, life expectancy is not altered.⁸ It may occasionally be confused with other causes of arterial occlusion so it is appropriate to have clinical, radiological and histological evidence for a definite diagnosis to be made.⁴ Sympathectomies are helpful in some patients; bypass surgery and anticoagulation are not.⁹

The management of the ischaemic pain in the affected limbs is not mentioned in most recent reviews of the disease. Our patient suffered severe pain in the affected digit which could not be controlled adequately despite large doses of opioids and other therapies. The long-term median nerve block enabled her to be discharged from hospital, and the selective blockade permitted her to use her crutches effectively. In this case the general practitioner was able to arrange for daily top-ups of local anaesthetic through the catheter. However, a constant infusion of local anaesthetic using a portable infusion pump could also have been considered if the analgesia had not been effective for such a long period.

The need for delayed surgical intervention to allow a good line of demarcation between viable and non-viable tissue is not uncommon in patients with Buerger's disease. Insertion of a silastic catheter for prolonged regional nerve block should always be considered in order to avoid the long-term use of opioids.

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References

1. LOFSTROM B. Nerve block at the elbow. In: ERIKSSON E. ed. *Illustrated handbook in local anaesthesia*, 2nd edn. London: Lloyd Luke, 1979: 88.
2. VON WINIWARTER F. Über eine eigenthümliche Form von Endarteriitis und Endophlebitis mit Gangran des Fusses. *Archiv für klinische Chirurgie* 1879; **23**: 202-26.
3. BUERGER L. Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. *American Journal of the Medical Sciences* 1908; **136**: 567-80.
4. MORRIS-JONES W, JONES CDP. Buerger's disease in women. A report of a case and a review of the literature. *Angiology* 1973; **24**: 675-90.
5. DU TOIT DF, MARITZ J, KLONPJE J, LAKER L, GROENEWALD JH. Buerger's disease. A case report and review of the literature. *South African Medical Journal* 1984; **66**: 701-2.
6. LEAVITT RY, BRESSLER P, FAUCI AS. Buerger's disease in a young woman. *American Journal of Medicine* 1986; **80**: 1003-5.
7. WESSLER S. Buerger's disease revisited. *Surgical Clinics of North America* 1969; **49**: 703-13.
8. EASTCOTT HHG. *Arterial surgery*, 2nd edn. London: Pitman Medical Publishing, 1973: 96-112.
9. WELLING RE. Buerger's disease revisited. *Angiology* 1982; **33**: 239-50.

CASE REPORT

Sick sinus syndrome manifest after spinal anaesthesia

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Summary

A case of sick sinus syndrome which presented as a cardiac arrest following spinal anaesthesia is reported. The diagnosis of sick sinus syndrome, the cardiovascular effects of spinal anaesthesia and the anaesthetic management of patients with the syndrome are discussed.

Key words

*Anaesthetic techniques, regional; spinal.
Heart; sino-atrial node*

The presentation of sick sinus syndrome is varied and ranges from patients who are asymptomatic to those with cardiac arrest of variable duration. We describe a patient in whom the diagnosis was made when she had a cardiac arrest on the ward several hours after spinal anaesthesia.

Case history

A 46-year-old woman presented for bilateral high tie and stripping of varicose veins. She had received one previous uneventful general anaesthetic for tonsillectomy. She suffered from premenstrual tension and insomnia for which she took lorazepam 0.5–1.0 mg daily. She denied any cardiovascular symptoms. Pre-operative examination of respiratory and cardiovascular systems was unremarkable. Her arterial blood pressure was 145/95 mmHg and she had a regular pulse of 70 beats/minute.

She received diazepam 10 mg orally 90 minutes pre-operatively. An intravenous infusion of Hartmann's solution was begun before a spinal injection was performed via a 25-gauge needle at the level of L₃₋₄ with the patient in the left lateral position. She was positioned supine after injection of 2.5 ml 0.5% heavy bupivacaine. Loss of pinprick sensation occurred up to the T₁₀ dermatome.

She felt no discomfort but was rather anxious so a total of 5 mg midazolam was administered intravenously over the next half-hour. Peroperative pulse and arterial blood pressure remained stable at 65–75 beats/minute and 90–95 mmHg systolic, respectively. The electrocardiograph (ECG) remained normal until 90 minutes after the spinal injection, when the heart rate decreased to 48 beats/minute although she remained in sinus rhythm. The arterial pressure was then

70 mmHg systolic and the patient was asymptomatic. Atropine 0.6 mg intravenously did not produce any change in heart rate, which increased 10 minutes later to 70 beats/minute with a systolic arterial pressure of 90 mmHg.

The operation lasted for 2 hours 15 minutes, when she was transferred to the recovery area where her blood pressure was 110 mmHg systolic and pulse rate 80 beats/minute. She returned to the surgical ward 3 hours after the spinal injection.

The patient complained after a further 3 hours that she felt faint with pain in the left axilla. Nursing staff reported that she lost consciousness, was very pale and her pulse was not palpable. The episode lasted about 20 seconds and rapid recovery followed two blows to the chest. Examination of the patient and 12-lead ECG revealed no evidence of the cause of collapse. She was in sinus rhythm with a pulse rate of 75 beats/minute and arterial pressure 110/70 mmHg. A chest X ray was normal. An urgent lung scan was performed in order to exclude a diagnosis of pulmonary embolism. She again felt faint after the injection of technetium and her pulse became weak, though palpable. Rapid spontaneous recovery ensued. The perfusion scan did not suggest pulmonary embolism so she was transferred to a medical ward.

She again felt unwell 2 hours later, 8 hours after the spinal injection, and became pale and sweaty. An ECG monitor showed a short period of asystole. External cardiac massage was required for about one minute before there was an abrupt return of cardiac output and consciousness. An isoprenaline infusion was started and the patient transferred to the coronary care unit in another hospital in the city.

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Her pulse rate on arrival was 120 beats/minute; the isoprenaline was discontinued and the ECG monitored continuously. Serum electrolytes were normal. Four hours elapsed before the pulse rate decreased to 60 beats/minute, when she complained of nausea. The monitor then showed sinus arrest which was terminated by a blow on the chest. A temporary pacing wire was inserted via the left subclavian route and later a permanent device replaced it.

Direct questioning revealed several previous blackouts, usually related to vomiting; the most recent had occurred 8 months earlier. A diagnosis of sick sinus syndrome was made. She was discharged from hospital well, 4 days post-operatively. A 24-hour ECG tape at follow up showed sinus rhythm with a minimum heart rate of 54 beats/minute. There were occasional ventricular ectopics and one episode of sinus tachycardia (160 beats/minute). She had no further attacks of syncope.

Discussion

The sick sinus syndrome encompasses a heterogeneous group of disturbances of cardiac rhythm attributable to sinus node dysfunction. Lown¹ first used the term 'sick sinus' to describe a condition in which chaotic atrial activity followed electrical cardioversion. Ferrer² then grouped all dysrhythmias due to sinus node dysfunction together under the general heading of sick sinus syndrome. This included sinus bradycardia, sinus arrest of varying duration followed by atrial or junctional escape rhythms or cardiac arrest, untreated chronic atrial fibrillation with a slow ventricular rate, inability to resume sinus rhythm after cardioversion and sino-atrial block. Episodic supraventricular tachydysrhythmia may also be included and the syndrome is then called tachycardia-bradycardia syndrome.³

It is difficult to ascertain the incidence of sick sinus syndrome because it is not clearly defined but a large survey between 1968 and 1976 showed that 0.05% of the population had potential or established sino-atrial disorders.⁴ Sick sinus syndrome is more common in males and older age groups⁴ although it does occur in young people, when a genetic factor may be involved,⁵ and in children, when it is likely to follow cardiac surgery or in association with congenital heart disease or myocarditis.⁶ The cause of the syndrome remains unknown but patients with a sick sinus show loss of specialised atrial muscle cells and the node is largely replaced by fibrous tissue, a process which can be due to ageing. Coronary artery disease, as defined by angiography, does not correlate with sick sinus syndrome; indeed, the sinus node artery is frequently spared when arteriosclerosis co-exists with sick sinus syndrome.⁷

Diagnosis may be difficult because patients present with a variety of symptoms that include syncope, dizziness, palpitations and angina, or with signs of heart failure or cerebrovascular events. The ECG at presentation is frequently normal. The patients may alternatively be asymptomatic and the diagnosis made coincidentally from the ECG. A 24-hour ambulatory ECG increases the likelihood of detecting dysrhythmias in those with a normal 12-lead ECG. Some simple tests have been used in an attempt to make a bedside diagnosis. Patients with sick sinus syndrome do not demonstrate the normal increase in heart rate during the strain phase of the Valsalva manoeuvre or the decrease during the post-Valsalva blood pressure overshoot, and carotid sinus massage produces a decrease

in heart rate which may result in sinus arrest for 3–6 seconds.⁸ The response to exercise or isoprenaline in patients with sick sinus syndrome may be normal. The increase in heart rate following atropine is diminished, as with this patient; the rate does not increase above 90 beats/minute even in patients who show some response.⁹

Electrophysiological tests have been used in an attempt to clarify the parts played by intrinsic sinus node dysfunction and autonomic tone. These tests are invasive but studies have been undertaken on small numbers of patients with sick sinus syndrome. Measurement of intrinsic heart rate following autonomic blockade with propranolol and atropine is followed by measurement of sino-atrial conduction time and sinus node recovery time after atrial pacing.^{10–12} It is possible to categorise patients into two main groups on the basis of results from these studies: those with intrinsic sinus node disease and those with disturbed autonomic regulation. The former have abnormal intrinsic heart rates and sinus node recovery times. The latter have normal intrinsic heart rates and decreased sino-atrial conduction times after autonomic blockade, which suggests enhanced basal parasympathetic tone; increased sino-atrial conduction times in a number of cases suggest enhanced sympathetic tone that masks an underlying intrinsic abnormality.

Spinal anaesthesia has cardiovascular effects produced by sympathetic blockade which extends beyond the level of the sensory block by 2–6 segments.¹³ This is because the smaller sympathetic nerve fibres are more sensitive to local anaesthetic than the larger sensory ones and because the concentration of local anaesthetic decreases with distance from the site of injection. Also, preganglionic sympathetic fibres ascend and descend in the paravertebral chain, so that blocking one preganglionic fibre produces a diffuse peripheral sympathetic response that extends beyond the affected sensory dermatomes.

Bradycardia and hypotension may be associated with spinal anaesthesia. Subarachnoid injection of 3 ml 0.5% hyperbaric bupivacaine resulted in peak plasma levels of 35–100 ng/ml at 40–75 minutes with an apparent elimination half-life of 1.7–4.7 hours.¹⁴ The plasma concentrations of bupivacaine during spinal anaesthesia are unlikely to cause systemic effects, because they are well below the suggested safe level of 1.5 µg/ml.¹⁵ Hypotension during spinal anaesthesia is due in part to sympathetic blockade that produces vasodilatation. Some compensation occurs by vasoconstriction in the rest of the body but this is limited if the block is extensive. The extent of sympathetic paralysis determines venous return and hence cardiac output. Cardio-accelerator fibres are also involved if the block includes T₂–T₅, so that no compensatory tachycardia occurs; indeed, bradycardia can result since the vagal supply to the heart remains intact.

The balance between sympathetic and parasympathetic tone is important in the maintenance of heart rate and may be upset by blockade of the former by local anaesthetic agents during spinal anaesthesia or enhancement of the latter in sick sinus syndrome. It is possible that patients with sick sinus syndrome are unable to produce a tachycardic response to hypotension, even when sympathetic blockade is not extensive, and that those with enhanced parasympathetic tone are especially prone to bradycardia if the block is high. The diagnosis of sick sinus syndrome may thus be uncovered during spinal anaesthesia. The

occurrence of otherwise unexplained bradycardia unresponsive to atropine was the first pointer to the diagnosis in our patient.

The question of pacing arises once sick sinus syndrome has been diagnosed. Insertion of a pacemaker does not prolong survival¹⁶ but it may improve the quality of life. It has therefore been suggested that only symptomatic cases be paced. Those without a pacing wire who present for surgery with sick sinus syndrome may pose a problem for the anaesthetist, particularly if they have bradycardias that are unresponsive to chronotropic drugs. It is advisable to consider insertion of a temporary transvenous pacing wire in such patients whether general or spinal anaesthesia is administered, since bradycardic episodes may occur during either.¹⁷

References

1. LOWN B. Electrical reversion of cardiac arrhythmias. *British Heart Journal* 1967; **29**: 469–89.
2. FERRER MI. The sick sinus syndrome in atrial disease. *Journal of the American Medical Association* 1968; **206**: 645–6.
3. KAPLAN BM, LANGENDORF R, LEV M, PICK A. Tachycardia-bradycardia syndrome (so-called 'sick sinus syndrome'). *American Journal of Cardiology* 1973; **31**: 497–508.
4. SHAW DB, KEEWICK CA. Potential candidates for pacemakers. Survey of heart block and sinoatrial disorder (sick sinus syndrome). *British Heart Journal* 1978; **40**: 99–105.
5. MACKINTOSH AF. Sinoatrial disease in young people. *British Heart Journal* 1981; **45**: 62–6.
6. RADFORD DJ, IZUKAWA T. Sick sinus syndrome: symptomatic cases in children. *Archives of Disease in Childhood* 1975; **50**: 879–85.
7. ENGEL TR, MEISTER SG, FEITOSA GS, FISCHER HA, FRANKL WS. Appraisal of sinus node artery disease. *Circulation* 1975; **52**: 286–91.
8. MANDEL WJ, HAYAKAWA H, ALLEN HN, DANZIG R, KERMAIER AI. Assessment of sinus node function in patients with the sick sinus syndrome. *Circulation* 1972; **46**: 761–9.
9. ROSEN KM, LOEB HS, SINNO MZ, RAHIMTOOLA SH, GUNNAR RM. Cardiac conduction in patients with symptomatic sinus node disease. *Circulation* 1971; **43**: 836–44.
10. JORDAN JL, YAMAGUCHI I, MANDEL WJ. Studies on the mechanism of sinus node dysfunction in the sick sinus syndrome. *Circulation* 1978; **57**: 217–23.
11. DESAI JM, SCHEINMAN MM, STRAUSS HC, MASSIE B, O'YOUNG J. Electrophysiologic effects of combined autonomic blockade in patients with sinus node disease. *Circulation* 1981; **63**: 953–60.
12. KANG PS, GOMES JAC, KELEN G, EL-SHERIF N. Role of autonomic regulatory mechanisms in sinoatrial conduction and sinus node automaticity in sick sinus syndrome. *Circulation* 1981; **64**: 832–8.
13. GREENE NM. Area of differential block in spinal anesthesia with hyperbaric tetracaine. *Anesthesiology* 1958; **19**: 45–50.
14. BURM AG, VAN KLEEF JW, GLADINES MP, SPIERDIJK J, BREIMER DD. Plasma concentrations of lidocaine and bupivacaine after subarachnoid administration. *Anesthesiology* 1983; **59**: 191–5.
15. TUCKER GT, MATHER LE. Clinical pharmacokinetics of local anaesthetics. *Clinical Pharmacokinetics* 1979; **4**: 241–78.
16. SHAW DB, HOLMAN RR, GOWERS JI. Survival in sinoatrial disorder (sick-sinus syndrome). *British Medical Journal* 1980; **280**: 139–41.
17. BURT DER. The sick sinus syndrome. A complication during anaesthesia. *Anaesthesia* 1982; **37**: 1108–11.

CASE REPORT

Recurarisation following a suxamethonium–alcuronium sequence in patients with atypical cholinesterase

A. BARAKA, A.-N. SIBAI, M. HAMED AND R. DELLEH

Summary

Alcuronium 10 mg was administered to maintain muscle relaxation in two patients before recovery from suxamethonium neuromuscular blockade to facilitate tracheal intubation. This sequence resulted in a markedly prolonged block which could not be antagonised adequately by neostigmine 0.05 mg/kg; initial antagonism was followed rapidly by prolonged recurarisation. Estimation of plasma cholinesterase activity revealed that the two patients were homozygous for the atypical and silent genes, respectively.

Key words

Enzymes; plasma cholinesterase.

Neuromuscular relaxants; alcuronium, suxamethonium.

Suxamethonium is rapidly hydrolysed by plasma cholinesterase¹ and is therefore used widely to provide a short period of profound neuromuscular blockade which facilitates tracheal intubation. Muscular relaxation is usually maintained by a long-acting, non-depolarising relaxant administered after recovery from suxamethonium blockade but, on occasion, the relaxant is administered prior to recovery from suxamethonium in an attempt to avoid bucking and straining. The following two case reports illustrate the fact that this technique masks prolonged suxamethonium blockade in patients with atypical plasma cholinesterase and can result in a markedly prolonged block which is difficult to antagonise with neostigmine.

Case histories

Case 1

A 60-year-old female, body weight 70 kg, was scheduled for fixation of a tibial fracture. Anaesthesia was induced with thiopentone 5 mg/kg and suxamethonium 100 mg. Anaesthesia was maintained with nitrous oxide–oxygen following tracheal intubation. Alcuronium 10 mg to maintain muscle relaxation was injected prior to recovery from suxamethonium blockade. Complete relaxation was achieved throughout the operative procedure, which lasted for 60 minutes. The patient was transferred, intubated, to the recovery room where controlled ventilation was continued.

Neuromuscular transmission was monitored by electromyography (Datex). The ulnar nerve was stimulated supramaximally at the wrist every 20 seconds and the resulting electromyographic response displayed. The monitor uses the train-of-four principle at a stimulation rate of 2 Hz, and features an automatic search for the supramaximal stimulus. The monitor computes the ratio of the fourth to the first evoked response (T_4/T_1 ratio). Spontaneous recovery of neuromuscular transmission began after 150 minutes of complete neuromuscular blockade. A mixture of neostigmine 0.05 mg/kg and atropine 0.02 mg/kg was injected to antagonise neuromuscular blockade when the train-of-four response revealed a T_4/T_1 ratio of 0.25. As shown in Fig. 1, the injection of neostigmine was followed by initial antagonism as evidenced by a T_4/T_1 ratio of 1.0. However, this was followed rapidly by recurarisation. Adequate and sustained recovery of neuromuscular trans-



Fig. 1. Electromyographic recordings showing the biphasic response to neostigmine 0.05 mg/kg. Initially, neostigmine antagonised the block and increased the T_4/T_1 ratio from 0.25 to 1.0. However, this was followed rapidly by a second phase of recurarisation.

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mission was achieved only after a further 120 minutes, when the patient's trachea was extubated.

A blood sample was taken to estimate plasma cholinesterase because of the unexpectedly prolonged neuromuscular blockade and the inadequate reversal by neostigmine following a normal dose of alcuronium, to investigate the possibility of prolonged suxamethonium block which was masked by alcuronium administered before recovery from suxamethonium. Plasma cholinesterase was determined using propionylthiocholine as substrate. The control value in our population² is 4.1–1.4 iu/ml. The plasma cholinesterase in the patient was 0.76 iu/ml and the dibucaine number (DN) was 30, which indicates that the patient was homozygous for the atypical dibucaine resistant gene ($E_1^*E_1^*$).

Case 2

A 42-year-old multigravida, body weight 80 kg, was scheduled for Caesarean section. Anaesthesia was induced with thiopentone 3 mg/kg and suxamethonium 100 mg, and maintained with nitrous oxide–oxygen following tracheal intubation. Alcuronium 10 mg was injected prior to recovery from suxamethonium. No additional alcuronium was required until the end of surgery, which lasted 75 minutes. Antagonism of neuromuscular blockade was attempted with a mixture of neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Adequate spontaneous breathing was observed clinically following reversal and the patient's trachea was extubated. However, the patient complained of difficulty in breathing and became cyanosed after 10 minutes. The trachea was re-intubated and ventilation controlled for 2 hours, when the patient resumed adequate spontaneous breathing and the trachea could be extubated.

As in the previous patient, prolonged suxamethonium blockade was suspected. The plasma cholinesterase activity of the patient was 0.1 iu/ml and the dibucaine number could not be estimated because of the very low cholinesterase activity. This suggests that the patient was homozygous for the silent gene ($E_1^*E_1^*$).

Discussion

There are no pharmacological reasons to condemn the use of suxamethonium to facilitate tracheal intubation followed by a non-depolarising muscle relaxant to maintain relaxation once adequate recovery from suxamethonium blockade has been confirmed.^{3,4} The injection of non-depolarising muscle relaxant prior to recovery from suxamethonium,

as illustrated by our two patients, can mask prolonged suxamethonium blockade in patients with atypical plasma cholinesterase, and results in a mixed neuromuscular block secondary to both depolarising and non-depolarising blockade. Markedly prolonged and complete neuromuscular block followed a suxamethonium–alcuronium sequence in these two patients. Neostigmine could not antagonise the block adequately but resulted in a biphasic response. Neuromuscular blockade was initially antagonised but this was followed rapidly by a second phase of prolonged recurarisation which lasted for 1–2 hours. The initial phase can be attributed to antagonism of the non-depolarising blockade due to alcuronium, while recurarisation may be secondary to potentiation of suxamethonium blockade by neostigmine.^{5,6}

In conclusion, the present report shows that the injection of a non-depolarising relaxant prior to recovery from suxamethonium blockade can mask negligible hydrolysis of suxamethonium in patients with atypical plasma cholinesterase activity, and result in markedly prolonged neuromuscular blockade which is difficult to antagonise by neostigmine. Atypical esterase activity must be suspected whenever unduly prolonged neuromuscular blockade follows a suxamethonium–non-depolarising relaxant sequence.⁷ The report also supports the traditional teaching that non-depolarising relaxants must be administered only after recovery from suxamethonium blockade has been ensured.^{3,4}

References

1. KALOW W. The distribution, destruction and elimination of muscle relaxants. *Anesthesiology* 1959; **20**: 505–18.
2. WAKID NW, TUBBEH R, BARAKA A. Assay of serum cholinesterase with succinylcholine and propionylthiocholine as substrates. *Anesthesiology* 1985; **62**: 509–12.
3. FELDMAN SA. The rational use of relaxants. Mixing relaxants. In: FELDMAN SA, ed. *Muscle relaxants (Major problems in anaesthesia, Vol. 1)*. W.S. Saunders Company Ltd, 1973: 156–7.
4. CHURCHILL-DAVIDSON HC. Neuromuscular blocking drugs. Mixing of relaxants. In: CHURCHILL-DAVIDSON HC, ed. *A practice of anaesthesia*, 4th edn. London: Lloyd-Luke, 1978: 902–3.
5. BARAKA A. Potentiation of suxamethonium blockade by neostigmine in patients with atypical cholinesterase. *British Journal of Anaesthesia* 1975; **47**: 416–8.
6. PAYNE JP, HUGHES R, AL AZAWI S. Neuromuscular blockade by neostigmine in anaesthetized man. *British Journal of Anaesthesia* 1980; **52**: 69–76.
7. DYKES MHM, CHENG SC, COHEN H, VALLE RF. Multiple neuromuscular blocking agents and reversal in a patient with absent plasma cholinesterase. *Canadian Anaesthetists' Society Journal* 1986; **33**: 657–61.

Tracheal tube cuff pressure

Clinical use of the Cardiff Cuff Controller

B. A. WILLIS, I.P. LATTO AND A. DYSON

Summary

Seventy-one adult patients (31 male, 40 female) who presented for surgery underwent orotracheal intubation with Portex Blue Line standard cuff disposable tubes (9-mm for males, 8-mm for females). The tracheal tube cuff was inflated by a trained assistant using a syringe and the initial cuff pressure measured; the minimum cuff pressure required to prevent respiratory gas leakage was also measured and the cuff pressure maintained above this pressure throughout the operation by means of the Cardiff Cuff Controller. Initial cuff pressure values averaged 11.9 kPa for males and 13.5 kPa for females compared with minimum cuff pressure values of 5.2 and 1.2 kPa, respectively. The differences between initial and minimum pressures were statistically highly significant ($p \leq 0.001$). It is concluded that the present method of inflation may lead to gross overinflation of tracheal tube cuffs and that cuff pressure monitoring may be performed simply by means of an electropneumatic controller. The difference in minimum cuff pressure between males and females suggests that the difference in tracheal size between the sexes is greater than the 9-mm to 8-mm difference in tracheal tube size.

Key words

Equipment; cuffs, tracheal.

The inflatable cuff of a tracheal tube has two functions. It should prevent aspiration of pharyngeal contents into the trachea and it should allow leak-free positive pressure ventilation. It is widely known that excessive pressure on the tracheal mucosa can result in trauma¹ and many methods of cuff management and types of cuff design have been described² in order to minimise this. Measurement of cuff pressure is rarely performed in British anaesthetic practice³ but such measurements may help to prevent accidental overinflation. In order to assess the degree of overinflation it was decided to measure cuff pressures generated during routine clinical practice and also to measure the minimum cuff pressure required to produce a leak-free tracheal seal in the same patients.

The aims of the present study were thus two-fold: to assess syringe inflation of the tracheal tube cuff by measuring the initial cuff pressure (ICP) after inflation by a trained assistant; and to measure the minimum cuff pressure (MCP) compatible with the absence of leakage past the cuff as detected by auscultation over the trachea.

Methods

Two instruments were used, the first measured and the second measured and controlled. The measurement of ICP was by a portable battery-powered pressure transducer (ICT series 1800) with built-in amplifier and digital display.

The transducer has a low compliance with a small internal volume (150 μ l) so that connexion to a previously inflated cuff enables the pressure within the cuff to be determined. The response is linear over the range 0–26.6 kPa and a built-in reference voltage enables the calibration to be checked. The second instrument, the Cardiff Cuff Controller,⁴ is an electropneumatic device which incorporates the same pressure transducer for measurement but it has an additional facility to maintain a constant tracheal tube cuff pressure at a preset value in the range 0.7–20 kPa. Both these instruments were calibrated against a mercury manometer over the range 0–26.6 kPa and were linear to within 0.133 kPa over this range.

Seventy-one patients scheduled to undergo elective surgery were studied and their tracheas were intubated after induction of anaesthesia and muscle paralysis. Portex Blue Line orotracheal, disposable tubes with standard cuffs were used, 9-mm for adult males and 8-mm for adult females; the cuff was inflated by a trained assistant using a 10-ml syringe via a three-way tap. Air was injected until no gross leakage was audible. Neither of the instruments was connected to the tracheal tube at this stage in order that the normal routine was not influenced in any way.

The initial cuff pressure (ICP) was measured using the low-compliance transducer after which the Cardiff Cuff Controller was connected and set at 4.0 kPa. If no leak was present at 4.0 kPa the minimum cuff pressure (MCP) was

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measured while the cuff pressure was reduced slowly until a leak was first detected by auscultation over the trachea. The system pressure was returned to 4.0 kPa after the MCP was measured. If an audible leak occurred the system was inflated until the leak disappeared (giving the MCP) and left at 0.7 kPa above this value. Leaks were tested for intermittently during the procedure. The cuff pressure was adjusted to eliminate any leaks that developed during an anaesthetic.

Results

The distribution of ICP and MCP values in males is shown in Fig. 1, for females in Fig. 2 and for all cases in Fig. 3. ICP values averaged 11.9 kPa for males and 13.5 kPa for females, compared with MCP values of 5.2 and 1.2 kPa, respectively. The overall mean ICP was 12.8 kPa (SEM 0.7) and overall mean MCP, 2.9 kPa (SEM 0.35). There was a highly significant difference in each case between ICP and MCP (paired Wilcoxon rank test and paired *t*-test).

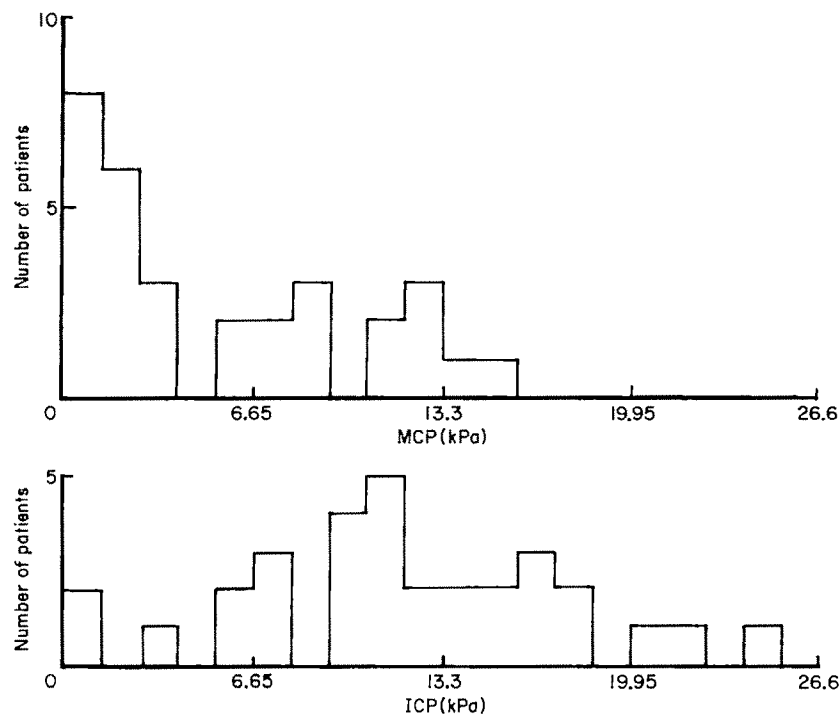


Fig. 1. MCP and ICP for males.

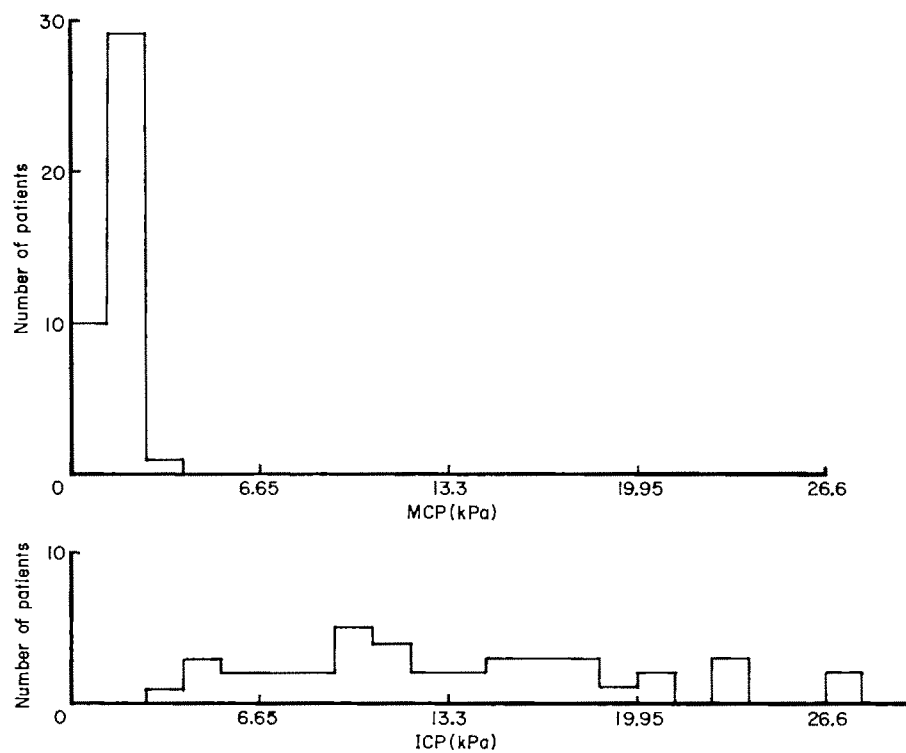


Fig. 2. MCP and ICP for females.

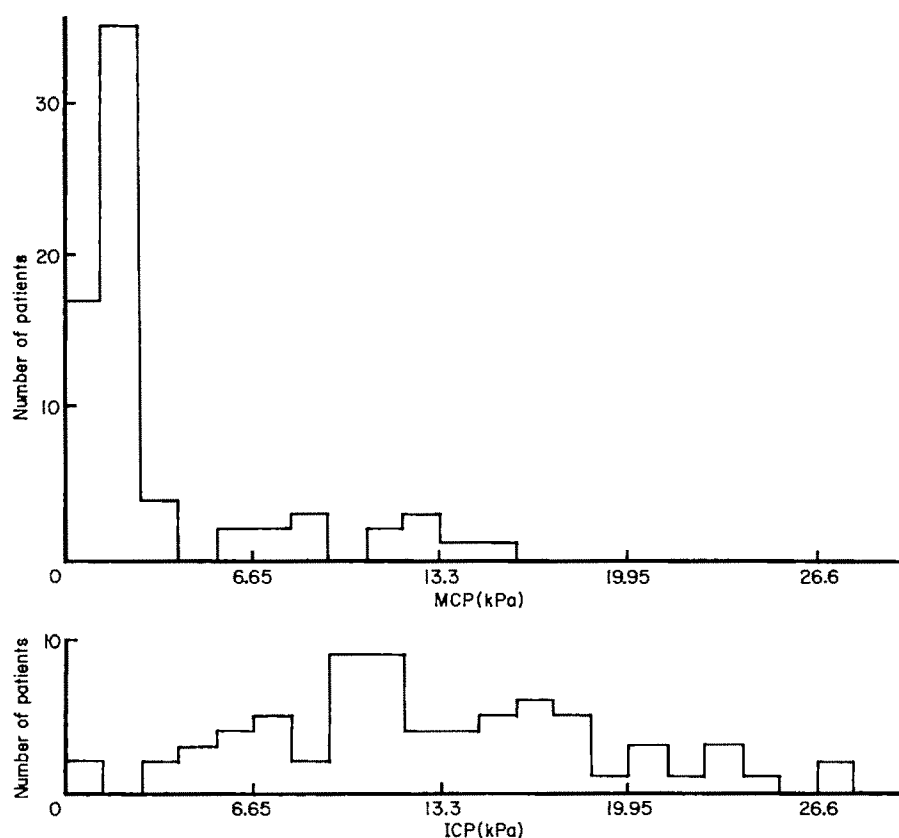


Fig. 3. MCP and ICP for all cases.

Discussion

It is apparent that syringe inflation of a tracheal tube cuff may produce a grossly overinflated cuff. Instructions to the assistant should be just to eliminate the leak and the temptation to add additional volume for good measure resisted. Display of cuff pressure during inflation has been recommended¹ and should help to prevent such gross overinflation of the cuff.

The Cuff Controller was found to be simple to use, in that it involves only one connexion to the cuff inflation port, and reliable in operation; it maintained cuff pressure at the preselected values throughout the operation.

It is interesting that no adult females intubated with an 8-mm tracheal tube required a pressure greater than 4.0 kPa to eliminate leakage past the cuff (mean MCP 1.2 kPa), whereas the wide range of MCP values in adult males intubated with a 9-mm tube suggests that, in some cases, the use of a larger tube would have led to lower values of

MCP, that is, the difference in tracheal size between adult males and females is greater than the 9-mm to 8-mm tube-size difference used in this study. A further study is in progress to determine ICP and MCP with Portex Profile cuffed tubes.

References

1. SEEOBIN RD, VAN HASSELT GL. Endotracheal cuff pressure and tracheal mucosal blood flow: endoscopic studies of effects of four large volume cuffs. *British Medical Journal* 1984; **288**: 965-8.
2. LATTO IP, ROSEN M, eds. *Difficulties in tracheal intubation*. Eastbourne: Ballière Tindall, 1985.
3. PIPPIN LK, SHORT DH, BOWES JB. Long-term tracheal intubation practice in the United Kingdom. *Anaesthesia* 1983; **38**: 791-5.
4. MORRIS JV, LATTO IP. An electropneumatic instrument for measuring and controlling the pressures in the cuffs of tracheal tubes: 'the Cardiff Cuff Controller'. *Journal of Medical Engineering and Technology* 1985; **9**: 229-30.

Free radicals

Formation, function and potential relevance in anaesthesia

D. ROYSTON

Summary

Free radical species are ubiquitous in plant and animal life. This article describes briefly the formation of certain oxygen-centred free radicals which are essential for aerobic metabolism and host defences in humans. The mechanism of cytotoxicity of excess or inappropriate free radical production is described. The potential relevance of free radical tissue injury to the anaesthetist is illustrated using oxygen toxicity, adult respiratory distress syndrome and halothane hepatitis as examples.

Key words

Oxygen; toxicity, free radicals.

Lung; respiratory distress syndrome.

There is now a considerable and growing interest in the role of free radicals in a number of potentially noxious processes which may have direct relevance in clinical situations related to anaesthetic practice. The importance of free radical reactions in such diverse industries as food preservation and print and rubber has been known for some time. However, only recently has the involvement of free radicals in normal body chemistry been appreciated by the clinician.

The purpose of this article is to highlight the place of free radicals in three areas. Firstly, to describe the process by which radicals are produced and to define the nature of free radicals and their reactions; secondly, to outline the relevance of free radical reactions in certain disease processes which are peculiar to anaesthesia and intensive care; and thirdly, to describe very briefly certain free radical injuries which have potential implications for anaesthetic practice.

Free radicals

Definition

A free radical is an atom or molecule which is capable of independent existence and which has one or more unpaired electrons. (An unpaired electron is one that occupies an atomic or molecular orbital by itself.) The presence of the unpaired electron sometimes makes the free radical species highly reactive and potentially cytotoxic, an effect that is used to kill bacteria by phagocytic cells, white cells and macrophages.

It is important to understand the reason for the production of such species in controlling our existence. This may be illustrated by the examples of aerobic metabolism and antibacterial defences.

Aerobic metabolism

One of the fundamental necessities for life is the ability to oxidise substrates in a controlled, efficient manner to produce high energy phosphates (specifically adenosine triphosphate, ATP). In outline, this process involves a wide range of substances, principally glucose, fatty acids and amino acids that are oxidised with the liberation of electrons and hydrogen ions, so-called 'reducing equivalents'. These are accepted by intracellular substances, principally nicotinamide adenine dinucleotide (NAD). Nature has developed a clever, if complex, system to allow the slow release of the energy contained in these electrons which are passed down a special transport system of flavoproteins and cytochromes to liberate their energy as ATP while at the same time regenerating NAD to be used again. This latter chain takes the reducing equivalents obtained from the substrate and passes them to a terminal receptor. In aerobic metabolism the terminal receptor is oxygen.

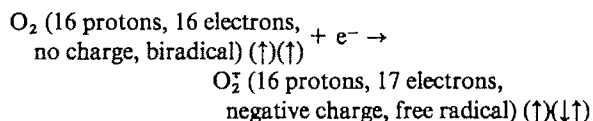
Reduction of molecular oxygen

Oxygen shares with selenium an ability to accept electrons one at a time. This reduction in singly controlled steps, makes oxygen a very appropriate receptor for the electrons and protons of the reducing equivalents.

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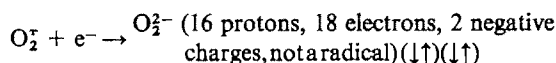
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Molecular oxygen (O_2) contains two unpaired electrons in its outer orbital. These electrons have parallel spins, i.e. $(\uparrow)(\uparrow)$. If the oxygen molecule is to take part in a chemical reaction then its next most stable configuration is to accept two further electrons into these outer orbitals. The additional electrons must spin in the opposite direction to those already in place to fulfill the requirements of the natural laws of physics and chemistry, and so the final configuration is $(\uparrow\downarrow)(\uparrow\downarrow)$. If this reaction occurred in one stage the oxygen would have to react with a substance whose two outer electron spins were also parallel. Such compounds are extraordinarily rare in nature. The special outer orbital configuration of oxygen therefore imposes a restriction on the molecule so that electrons have to enter the outer shells one at a time. The first stage is:



The species O_2^- is called superoxide.

The next stage of electron acceptance is:



The O_2^{2-} ion is termed the peroxide species and at physiological pH it is protonated to produce hydrogen peroxide (H_2O_2), an electrically neutral, stable compound. It is clear that free radicals must be produced during aerobic metabolism.

Production of free radicals during cell respiration

The mitochondrial mechanism of flavoproteins and cytochromes which controls cell respiration has the ubiquinone or coenzyme Q_{10} system at a pivotal early stage. The ability of oxygen to accept electrons singly is used to control the reaction in this early part of the respiratory chain; however, a free radical has to be produced as shown diagrammatically in Fig. 1.

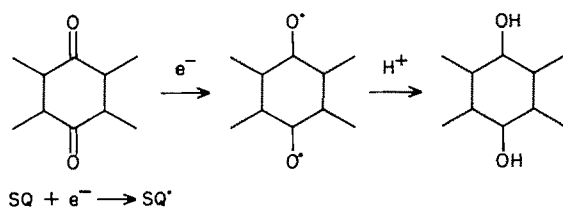
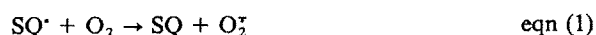


Fig. 1. Diagrammatic illustration of reduction and protonation of semiquinone (SQ) portion of oxidative phosphorylation to show free radical intermediary ($SQ^{\bullet -}$).

The Q_{10} system has a cyclic compound at its centre (a semiquinone, SQ). The oxygen on this substance can accept electrons singly to produce a free radical which is subsequently protonated. In this way the energy in the reducing equivalent electrons and protons can be released in a controlled manner. However, in normal metabolically active tissue there is a slow but constant production of superoxide anion, generated as a result of a side reaction between the semiquinone free radical ($SQ^{\bullet -}$) and molecular oxygen:



It must be emphasised, however, that by far the majority of electrons bypass this ubiquinone system and are passed directly onto oxygen using the complex and as yet not completely understood cytochrome oxidase system.¹ This system allows electrons to be passed along a chain while any free radical intermediates are 'hidden' and their expression or leak into the cell cytoplasm is prevented. The mechanism by which this is achieved has yet to be worked out.

Production of free radicals by phagocytic cells

Free radicals are produced by the cell membrane of active phagocytic cells as part of their mechanisms for killing bacteria. This is achieved by membrane-bound enzymes (NADPH oxidase) which are able to shuttle electrons from an appropriate donor (possibly a quinone) to molecular oxygen at the cell surface:



The superoxide produced is then passed into the phagosome produced by invagination of the phagocyte cell membrane, to attack the foreign particle, usually a bacterium. This process of activation is termed the respiratory burst. An hereditary absence of this NADPH oxidase complex is seen in patients with chronic granulomatous disease. The circulating neutrophils in these patients recognise and phagocytose foreign particles such as bacteria but cannot destroy them. Patients with this abnormality suffer from recurrent infections.

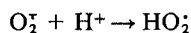
Other sources of oxidants and free radicals

By far the greatest number of free radicals and reduced oxygen species are produced during cell respiration and by activated phagocytic cells. However, there are other well-recognised reactions where reduced oxygen species are generated as by-products. In particular, superoxide production occurs at the endoplasmic reticulum and during the auto-oxidation of certain molecules such as catecholamines. There is also a growing interest in enzymes such as xanthine oxidase which can undergo molecular re-arrangement following a period of ischaemia. Molecular oxygen is converted to superoxide radical by the action of the re-arranged xanthine oxidase following reperfusion of the ischaemic organ.

Free radicals and oxidants derived from superoxide

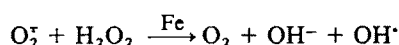
It is evident that the production of reduced species of oxygen and oxygen-derived free radicals is essential for bacterial killing and that these species are important in aerobic metabolism. So why have free radicals received recent attention because of their potential deleterious actions? This theory derives from their ability to oxidise cell components (by acting as an electron recipient) and thereby to produce a cytotoxic effect. Surprisingly, superoxide especially in aqueous solution, is relatively unreactive and acts as an electron donor (that is, a reducing agent) in the majority of its reactions. However, superoxide and hydrogen peroxide can react to produce free radicals and oxidant species of far greater destructive potential than the parent species.

In particular, the negative charge is lost if superoxide is protonated and the hydroperoxy radical (HO_2^\cdot) is formed:



This reaction is most likely to occur with high hydrogen ion concentrations; the pKa of the reaction is 4.8. This low pH is thought to occur in the phagosome and the hydroperoxy radical is thought to be the bacteriocidal species in this environment. The hydroperoxy radical is about 2×10^5 times more reactive than superoxide.

Superoxide can also react with hydrogen peroxide in the presence of metal cations (usually iron or copper) in the reaction:



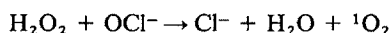
This is the so-called metal-catalysed Haber-Weiss reaction.

The hydroxyl free radical (OH^\cdot) has 9 protons and 9 electrons, is electrically neutral and has one of the electrons unpaired in an outer orbital. It is about 5×10^8 times more reactive than superoxide. Hydroxyl radical can also be generated directly by the effects of ionising radiation, such as radiotherapy dosage of X rays or gamma rays.

The iron-catalysed reactions require that the iron is in the ferrous (Fe^{2+}) form which is unlikely to occur in normal tissue: the vast majority of iron in the cells and plasma is in the oxidised (Fe^{3+}) form. However, in inflamed and damaged tissues it is possible to measure increased concentrations of Fe^{2+} iron, which suggests that the Haber-Weiss reaction may occur more readily.² The reduction of Fe^{3+} to Fe^{2+} can also be brought about by the action of superoxide radical:



Hydrogen peroxide can react with hypochlorous anion (produced in the phagocyte) to generate singlet oxygen ($^1\text{O}_2$):

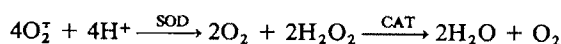


The molecular configuration of singlet oxygen is that of ground-state oxygen, namely 16 protons, 16 electrons with no charge. Its cytotoxic oxidant properties result from the configuration of the outer bonding electrons which are in an antiparallel spin ($\uparrow\downarrow$). This is a highly reactive configuration, some 2×10^8 times more than superoxide. Indeed, the hydroxyl free radical and singlet oxygen are so able to donate their electrons that they usually react indiscriminately with the first molecule they meet.

Finally, the use of the term free radical to describe singlet oxygen is not, by definition, correct. However, the term is used for brevity in most textbooks in preference to other more cumbersome terms such as reduced oxygen species.

Protection against free radicals

Anti-oxidant and free radical scavenging systems exist in order to protect against the damaging effects of free radicals produced as part of normal cell respiration and host defence. These systems are aimed at rapidly degrading superoxide anion (using superoxide dismutase, SOD) and hydrogen peroxide (using catalase, CAT) at their site of production, namely the mitochondrion and in the cell cytoplasm:



The injury which results from free radical attack is reduced and contained by other systems which use radical scavengers such as glutathione and anti-oxidants such as vitamin E. No enzyme systems which directly regulate the concentrations of hydroxyl radical or singlet oxygen are known to occur nor are there any naturally occurring scavengers of these highly reactive species. However, a number of compounds (e.g. caeruloplasmin) can bind transition metals (in this case copper) to prevent them taking part in the Haber-Weiss or similar reactions.

Tissue injury induced by free radicals.

A number of cell and tissue components are susceptible to free radical injury. The chemistry of reactions between free radicals and cell components is one of three main types: hydrogen abstraction, addition of the radical and electron transfer. These reactions illustrate a fundamental principle of free radical chemistry: the reaction of a free radical with a non-radical species produces a different free radical which may or may not be as reactive as the original species. Indeed, this is the mechanism of action of vitamin E. The complex tocopherol molecule is able to accept the odd electron from a radical into its structure without deleterious effect. This is shown diagrammatically in Fig. 2 for a

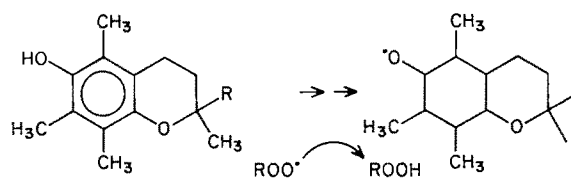


Fig. 2. Reaction of active centre of vitamin E molecule with a lipid peroxide radical (ROO^\cdot) to produce a nonreactive hydroperoxide (ROOH) and a vitamin E radical with very little reactivity.

reaction with a lipid peroxide (ROO^\cdot). Lipid peroxides are discussed further below.

Four components are specifically at risk of free radical injury: proteins, nucleic acids, membrane lipids and the supporting extracellular matrix. Proteins most at risk are those with amino acids that contain sulphur (methionine and cysteine). The free radical (e.g. hydroxyl) abstracts a proton and thereby oxidises the sulphhydryl moiety. Enzymatic proteins specifically at risk include α -1-antiprotease, calmodulin, calcium ATPase, glucose-6-phosphate dehydrogenase and glyceraldehyde phosphate-3-dehydrogenase.

Nucleic acids (specifically DNA) can be attacked either at the sugar-phosphate backbone or by addition into the purine or pyrimidine of the bases. The addition of hydroxyl radical to thymine is shown diagrammatically in Fig. 3.

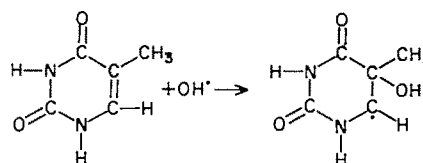


Fig. 3. Mechanism of hydroxyl radical injury to DNA base. Addition to thymine produces an unstable and relatively unreactive free radical.

The thymine free radical thus formed can undergo a number of reactions and degradations. However, the net result is to induce chromosomal deletions with subsequent cell death or mutation.

The unsaturated membrane lipids, which include cholesterol, can react readily with certain free radicals and undergo peroxidation. The peroxidation and eventual destruction of the polyunsaturated fatty acids (PUFAs) of the lipid membrane is shown diagrammatically in Fig. 4. In

of single collagen peptide chains to form triple-chain helices. This gelation can be prevented in the presence of systems that generate superoxide anion. In addition, free radicals can induce fragmentation and disruption of the proteoglycan polypeptides of the extracellular matrix.⁴

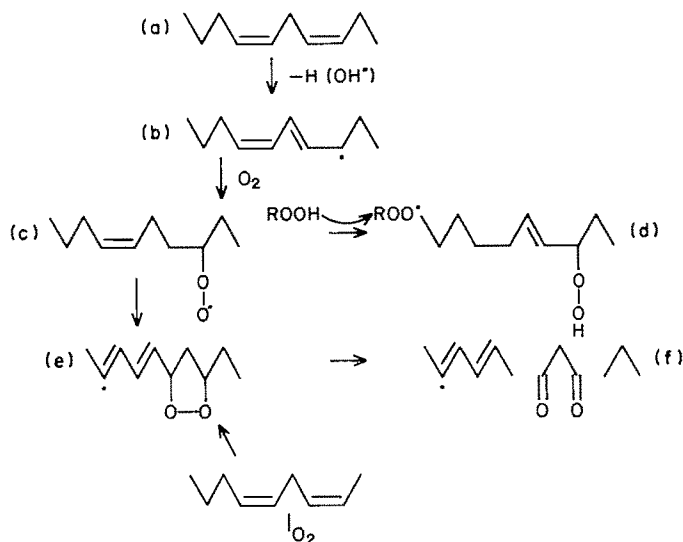


Fig. 4. Schematic representation of lipid peroxidation. (a) Polyunsaturated fatty acid; (b) conjugate diene; (c) lipid peroxide (also shown as ROO^\bullet); (d) lipid hydroperoxide (also shown as $ROOH$); (e) cyclic endoperoxide; (f) disrupted membrane lipid with release of malondialdehyde. Compound (e) is produced by the direct attack of singlet oxygen (1O_2). Compounds (c), (d), (e) and (f) are measured by the thiobarbituric acid (TBA) reaction.

brief, a hydrogen ion is abstracted from the PUFA by an oxygen-derived free radical (hydroxyl in the figure). The lipid free radical produced undergoes molecular re-arrangement to produce a conjugate diene, that is, a compound with two carbon-carbon double bonds separated by a carbon-carbon single bond. Conjugate dienes can be measured spectrophotometrically in body fluids and tissues. The conjugate diene can be converted into a lipid peroxide if the environment contains free molecular oxygen in appropriate amounts. The lipid peroxide (usually written as ROO^\bullet) can then either abstract a hydrogen ion from an adjacent molecule (forming a further free radical) to become a stable hydroperoxide, or it can undergo transformation to an unstable cyclic endoperoxide which is degraded to produce a number of compounds which include the three-carbon malondialdehyde. This dialdehyde is able to bind to and denature proteins. A possible consequence of the ability of lipid peroxides to transfer the radical electron in a chain reaction, may be that the free radical can 'travel' in the membrane and induce damage at a site remote from where it was produced. Cyclic endoperoxide may also be formed in the presence of singlet oxygen by direct addition across a double bond. The peroxides, hydroperoxides, cyclic endoperoxides and principally malondialdehyde form a coloured compound in a reaction with thiobarbituric acid (TBA) which can be measured spectrophotometrically and more accurately by fluorimetry. The TBA reaction has been the cornerstone of investigation into free radical dependent tissue lipid injury for the past three decades.³

Finally, the extracellular matrix can be injured by free radicals. The gelation of collagen involves the interaction

Free radical processes related to anaesthetic practice

Oxidants and free radicals have been implicated in a large number of disease processes such as carcinogenesis, atherosclerosis, arthritis and the process of ageing. What free radical processes are of specific relevance to the anaesthetist?

Pulmonary oxygen toxicity

The lung and pulmonary vasculature are potentially at higher risk of injury from oxygen-derived free radicals for a number of reasons. Firstly, the lung is exposed to higher concentrations of oxygen than any other organ in the body. Secondly, the administration of increased inspired oxygen concentrations during anaesthesia and on the intensive care unit to maintain adequate arterial oxygen tensions may increase the risk.

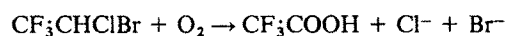
There is an increase in superoxide production under these hyperoxic conditions, by way of the side reaction of cell respiration outlined in eqn (1). There will also be a net increase in free radical activity if there is a relatively low concentration of the anti-oxidant enzymes superoxide dismutase and catalase which normally catalyse the degradation of this excess superoxide. Agents which reduce SOD and CAT concentrations in pulmonary tissue, such as steroids, or which increase tissue metabolic rate, such as catecholamines and thyroid hormones, augment the toxic effects of oxygen.⁵ Increase of SOD and CAT production or exogenous administration of these enzymes prior to challenge with hyperoxia reduces mortality due to oxygen toxicity in the laboratory rat.⁶

Acute lung injury associated with sepsis

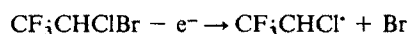
Another pulmonary insult which is thought to involve excess free radical production is the condition which is expressed clinically as the adult respiratory distress syndrome (ARDS): that is, a pulmonary injury secondary to a nonpulmonary disease. For example, a common predisposition to the development of ARDS is endotoxaemia and sepsis. Infusion of endotoxin in animal models is associated with the development of acute injury and an increase in lung lipid peroxidation products. The significant relationship between the degree of lung injury and amount of lipid peroxidation implies that oxidant free radicals play a part in this injury.⁷ Administration of SOD increases lung injury after challenge with endotoxin,⁸ in contrast to its protective effect in hyperoxia. However, and paradoxically, preliminary reports suggest that catalase protects against lung injury in the same animal model.⁹

Halothane hepatitis

Halothane hepatitis is a problem which may confront the anaesthetist and is possibly mediated by free radicals.¹⁰ About 20% of absorbed halothane in humans is metabolised by the cytochrome P450 system, by one of two pathways dependent on tissue oxygen tension. The cytochrome system in relatively hyperoxic states promotes oxidative degradation to stable trifluoroacetic acid:



The reductive pathway gains significance with decreased oxygen tensions. In this pathway cytochrome P450 removes an electron from halothane to produce a free radical; the bromine is lost from the molecule:



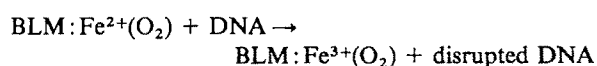
The $\text{CF}_3\text{CHCl}^\bullet$ radical has the same ability to abstract hydrogen from membrane PUFA as the CCl_3 radical derived from carbon tetrachloride (a well-known potent hepatotoxin). The sequence of events which follow the initial metabolic process with halothane thus depends greatly on the tissue oxygen tension; if it is high, oxidation occurs while if it is low, the free radical pathway is followed. However, the conjugate diene formed by abstraction from membrane PUFA (Fig. 4) cannot be oxidised if the tissue PO_2 is too low. Therefore there is no chemical disruption of the lipid and no lipid peroxidation. However, lipid peroxidation will follow if the oxygen tension is low enough to induce the free radical pathway but not entirely absent, and leads to cell membrane destruction and possibly cell death.

Treatment with xenobiotics

Other examples of injury mediated by free radicals in which the balance between oxygen tension and tissue injury may be important, are radiotherapy and following the administration of certain xenobiotics, in particular antitumour agents such as bleomycin, the herbicide Paraquat, the antibacterial nitrofurantoin and disulphuram (Antabuse). For example, Paraquat is activated to produce a Paraquat free radical (PQ^\bullet) which reacts with molecular oxygen to produce superoxide in the same way as the semiquinone system described earlier in eqn (1).¹¹ The superoxide can

then undergo transformation to more cytotoxic radicals as described previously. Hyperoxia increases the toxicity of Paraquat whereas breathing a hypoxic mixture may be protective. The lung is at particular risk since Paraquat is actively transported and concentrated within the pulmonary vascular endothelial cells.

Bleomycin (BLM) is a highly effective antitumour agent which acts by disruption of DNA (Fig. 3). It produces no toxic effect on the bone marrow, unlike other antitumour agents, but it may cause major adverse effects on the lung. The therapeutic action of bleomycin relies on the formation of an active complex with ferrous iron (Fe^{2+}) and possibly oxygen:



It seems logical to suppose that the toxic actions of bleomycin on the lung would be enhanced in the presence of an increased inspired oxygen concentration. This could be brought about by an increased production of superoxide radical (eqn (1)) which leads to the reduction of iron to the ferrous (Fe^{2+}) form (eqn (2)). Recent studies in laboratory animals have shown that brief (4-hour) exposures to high oxygen concentrations (90%) induce a significant pulmonary inflammatory response in animals previously given BLM.¹² There is still no consensus view as to the safe concentration of inspired oxygen to use during anaesthesia in patients who receive treatment with bleomycin.

A simple approach to the prevention of pulmonary injury associated with treatment with bleomycin or following injection of Paraquat, might be to give additional free radical scavengers. However, results from studies in laboratory animals have produced conflicting results. For example, the administration of *N*-acetyl cysteine (a synthetic analogue of the naturally occurring scavenger glutathione) reduces the mortality associated with oxygen exposure.¹³ However, in the same study the administration of *N*-acetyl cysteine to animals previously given Paraquat produced an increased mortality.¹³

Retinopathy of prematurity

The injury to the eye of neonates previously termed retrolental fibroplasia has also been ascribed to a free radical mechanism. Indeed, the two important risk factors in the development of this lesion are prematurity and the need for prolonged therapy with added oxygen.¹⁴ A number of papers have also reported that treatment with vitamin E may prevent the development of this retinopathy. However, more recent well-controlled trials showed that the administration of vitamin E is neither effective nor safe; treated babies had increased incidences of intraventricular haemorrhage and also necrotising enterocolitis.¹⁵

Conclusion

Free radicals and especially those centred on oxygen are ubiquitous in the body. We could not have aerobic metabolism and our bacteriocidal defences would be significantly lessened without the generation of free radical species. It may be, however, that free radicals are a double-edged sword and in either the wrong amount or in the wrong environment they may be deleterious and induce tissue injury. Therapy aimed at the reduction of this injury has

aimed to augment and increase anti-oxidant defences. This approach has shown promise with certain 'pure' insults such as oxygen toxicity, but it has not always produced the desired effect in more complex injuries such as sepsis and drug administration. The use of an inappropriate agent may amplify the injury and produce a deleterious effect in these more complex situations.

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References

1. CHANCE B, WILLIAMS GR. The respiratory chain and oxidative phosphorylation. *Advances in Enzymology* 1956; **17**: 65–73.
2. HALLIWELL B, GUTTERIDGE JMC. Oxygen toxicity, oxygen radicals transition metals and disease. *Biochemical Journal* 1984; **219**: 1–14.
3. CHANCE B, SEIS H, BOWERIS A. Hydroperoxide metabolism in mammalian organs. *Physiological Reviews* 1978; **59**: 527–605.
4. WOLFF SP, GARNER A, DEAN RT. Free radicals, lipids and protein degradation. *Trends in Biological Science* 1986; **11**: 27–31.
5. SMITH G. Oxygen toxicity. In: GRAY TC, NUNN JF, UTTING JE, eds. *General Anaesthesia*, 4th edn. London: Butterworths, 1980: 551–72.
6. TURRENS JF, CRAPO JD, FREEMAN BA. Protection against oxygen toxicity by intravenous injection of liposome-entrapped catalase and superoxide dismutase. *Journal of Clinical Investigation* 1984; **73**: 87–95.
7. DEMLING RH, LALONDE C, JIN L-J, RYAN P, FOX R. Endotoxaemia causes increased lung tissue lipid peroxidation in unanaesthetised sheep. *Journal of Applied Physiology* 1986; **60**: 2094–100.
8. TRABER DL, ADAMS T, SZIEBERT L, STEIN M, TRABER L. Potentiation of lung vascular responses to endotoxin by superoxide dismutase. *Journal of Applied Physiology* 1985; **58**: 1005–9.
9. MILLIGAN SA, HOEFFEL JM, FLICK MR. Endotoxin induced acute lung injury in unanaesthetised sheep is prevented by catalase. *American Review of Respiratory Disease* 1985; **131**: A422.
10. NEUBERGER J, WILLIAM R. Halothane anaesthesia and liver damage. *British Medical Journal* 1984; **289**: 1136–9.
11. SMITH LL. Mechanism of paraquat toxicity in lung and its relevance to treatment. *Human Toxicology* 1987; **6**: 31–6.
12. HAY JG, HASLAM PL, DEWAR A, ADDIS B, TURNER-WARWICK M, LAURENT GJ. Development of acute lung injury after the combination of intravenous bleomycin and exposure to hyperoxia in rats. *Thorax* 1987; **42**: 374–82.
13. PATTERSON CE, BUTLER JA, BYRNE FD, RHODES ME. Oxidant lung injury; intervention with sulphhydryl reagents. *Lung* 1985; **163**: 23–32.
14. BIGHAM AW, BROWN DR, MACPHERSON JA. Update on retinopathy of prematurity. *Seminars in Perinatology* 1986; **10**: 187–95.
15. PHELPS DL, ROSENBAUM AL, ISENBERG SJ, LEAKE RD, DOEY FJ. Tocopheral efficacy and safety for preventing retinopathy of prematurity; a randomised controlled, double-masked trial. *Pediatrics* 1987; **79**: 485–500.

Further reading

- FREEMAN BA, CRAPO JD. Biology of disease, free radicals and tissue injury. *Laboratory Investigations* 1982; **47**: 412–26.
- HALLIWELL B, GUTTERIDGE JMC. *Free radicals in biology and medicine*. Oxford: Clarendon Press, 1985.
- PRYOR WA. Oxyradicals and related species: their formation, lifetimes and reactions. *Annual Review of Physiology* 1986; **48**: 657–67.
- WEISS SJ. Oxygen, ischaemia and inflammation. *Acta Physiologica Scandinavica* 1986 (Suppl. **548**): 9–37.
- WEISS SJ, LO BUGLIO AF. Biology of disease: phagocyte generated oxygen metabolites and cellular injury. *Laboratory Investigation* 1982; **47**: 5–18.

Forum

Silent regurgitation in day case gynaecological patients

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Summary

The effect of metoclopramide premedication on the incidence of gastric regurgitation and postoperative nausea and vomiting was studied in 101 women during gynaecological procedures performed under mask anaesthesia. All patients were premedicated orally with carmine red and temazepam. A treatment group of 48 women also received oral metoclopramide. Anaesthesia was standardised in both groups. None of the women regurgitated gastric contents. Pharyngeal pH was measured in the last 68 patients and found to be >5 in all instances. Postoperative nausea and vomiting were significantly less frequent in the treatment group.

Key words

*Vomiting; antiemetics, metoclopramide.
Anaesthesia; outpatient.*

The loss of protective reflexes under general anaesthesia places patients at risk of aspiration of gastric contents should regurgitation occur. Silent regurgitation, which is recognised using a dye to colour the gastric contents, has been shown to occur in up to 26.3% of anaesthetised patients, of whom up to 76% aspirated.^{1–7} Day case patients may have an increased risk of aspiration following regurgitation when compared with a similar group of inpatients, since they have a significantly greater volume of gastric contents.⁸

Previous studies of regurgitation have not specifically considered day case patients and have used widely varying anaesthetic techniques. The purpose of this study was to determine the rate of silent regurgitation in gynaecological day case patients premedicated with temazepam and given a standardised anaesthetic. We also wished to determine whether the addition of metoclopramide to the premedication would alter the rate of silent regurgitation or postoperative nausea and vomiting.

Methods

We studied 101 patients who underwent day case gynaecological surgery. The trial was approved by the hospital's ethical committee, and the patients gave informed consent. Patients with a history of heartburn, hiatus hernia or other gastro-intestinal complaints were not studied.

The patients were allocated randomly to two groups and received oral premedication an estimated one hour before the induction of anaesthesia. The control group (53 patients) received temazepam 20 mg and carmine red 200 mg. The treatment group (48 patients) received temazepam 20 mg, carmine red 200 mg and metoclopramide 10 mg. Carmine red, a permitted food colouring,⁹ was used in previous studies to colour gastric contents.^{2–4} It was sterilised and packed in gelatin capsules.

Each patient's oropharynx was inspected for carmine red

before the induction of anaesthesia. Routine monitoring was established, an intravenous cannula inserted and fentanyl 25 µg followed by thiopentone 5 mg/kg injected. Further boluses of thiopentone 1 mg/kg were given if required to produce unconsciousness. Anaesthesia was maintained with 66% nitrous oxide, oxygen and halothane. Further increments of fentanyl 25 µg were injected during surgery as indicated clinically. None of the patients was intubated. The time the patients spent in different positions and the duration of surgery were recorded.

Pharyngeal toilet was performed at the end of surgery; secretions were aspirated under direct vision into a mucus trap. The pH of the aspirate was measured using fresh pH sensitive paper (Ames), range 2–5. The cause of any colouration of the aspirate was determined by addition of 10% ammonium hydroxide, which turns carmine red a reddish-purple colour and blood, brown. It became clear part way into the study that few patients had appreciable pharyngeal fluid, and so in the last 68 patients a fresh strip of pH sensitive paper was laid on the fluid that coated the hypopharynx.

The patients were discharged to the recovery room and from there to the day ward, where they and the nurses were asked whether nausea or vomiting occurred. The results were analysed using Student's *t*-test and the Chi-squared test with Yates' correction. The level of significance was taken as $p < 0.05$.

Results

There was no significant difference between the control and treatment groups with respect to age, weight or duration of anaesthesia (Table 1). None of the patients had carmine red in their pharynxes either before or after surgery, or pharyngeal fluid with pH < 5. We therefore conclude that regurgitation did not occur. Postoperatively the group

Table 1. Age, weight and duration of anaesthesia for each group. Values are means (SD).

	Control group (n = 53)	Treatment group (n = 48)
Age, years	25.6 (6.85)	26.3 (7.23)
Weight, kg	59.6 (10.3)	59.7 (10.2)
Duration of anaesthetic, minutes	12.6 (6.63)	12.3 (7.46)

Table 2. Number of patients with postoperative nausea and vomiting.

	Control group (n = 53)	Treatment group (n = 48)
Nausea alone	7	2
Nausea and vomiting	9	4*
Nausea or vomiting	16	6

* p < 0.05 compared to control group.

treated with metoclopramide suffered less from nausea or vomiting than the control group; this was statistically significant when these events were considered together (Table 2).

Discussion

The absence of regurgitation in this study agrees with the results of Fasano *et al.*,⁷ whose mask anaesthetised patients all had hypopharyngeal pH > 5.0. Our results do not mean that regurgitation will not occur; however, they compare favourably with results from other studies.

In Carlsson's study⁶ of gynaecological patients, whose lungs were ventilated, none of the elective cases (103) regurgitated. However, regurgitation occurred in 20% (7/35) of patients who underwent emergency laparoscopy. These patients may have had more disturbed gastrointestinal function than the elective patients. Duffy⁵ reported regurgitation in two of 93 patients who underwent day case laparoscopy that involved artificial ventilation. His patients received atropine and droperidol on induction of anaesthesia. Blitt *et al.*³ reported regurgitation in 4.4% of patients anaesthetised with a mask compared to 12.3% of patients whose tracheas were intubated. The use of muscle relaxants was associated with a 4.5 times increase in the incidence of regurgitation. Turndorf *et al.*⁴ found that regurgitation occurred in 5.1% (3/59) of spontaneously breathing, intubated patients and in 20% (19/93) of those whose lungs were ventilated. Both these workers and Blitt³ noted that regurgitation varied with patient position, but neither separated the effects of position and the mode of ventilation on the incidence of regurgitation.

Our patients had several factors which might predispose them to an increased risk of regurgitation. They would be expected to have twice the volume of gastric secretions compared to inpatients.⁸ The majority (64) were in the first trimester of pregnancy and would have a significant delay in gastric emptying compared to nonpregnant patients.¹⁰ Brock-Utne *et al.*¹¹ demonstrated a significant reduction of lower oesophageal barrier pressure in patients in the first trimester who complained of heartburn, and perhaps to a lesser extent even in those who did not. Our 22 patients who underwent laparoscopy were placed in a head-down lithotomy position and had gas injected into the peritoneal cavity, which increases the intra-abdominal pressure and so may increase the risk of regurgitation.

There are, however, other factors which may have prevented regurgitation. Unlike other investigators, we excluded patients who complained of heartburn. None of our patients was given an opioid premedication, which

delays gastric emptying¹² and decreases barrier pressure^{13,14} and may, like droperidol¹⁵ and atropine,¹⁶ increase the risk of regurgitation. Our patients were not given muscle relaxants so the cricopharyngeal sphincter may have remained functional and thus prevented regurgitation of any oesophageal fluid into the pharynx.¹⁷ The patients given metoclopramide, which increases the barrier pressure, would be further protected from regurgitation of gastric fluid into the oesophagus.¹⁵ Finally, none of our patients had a stormy induction of anaesthesia, which has been shown to be associated with an increased frequency of regurgitation.² The effects of benzodiazepines on lower oesophageal barrier pressure are variable,^{18,19} and those of lorazepam and temazepam unknown.

The reduction in postoperative nausea and vomiting agrees with the findings of Madej and Simpson.²⁰ The use of intravenous fentanyl as the sole narcotic by these workers and ourselves, may have reduced the time during which opioid induced nausea and vomiting occur. Most authors^{1-3,6,7} gave intramuscular opioids as part of their premedication. Duffy⁵ gave oral lorazepam, while Turndorf *et al.*⁴ do not state the premedication used.

In conclusion, regurgitation of gastric contents into the pharynx was sought in 101 gynaecological day patients premedicated with temazepam with or without metoclopramide. No regurgitation was detected and there was a significant reduction of postoperative nausea and vomiting in the metoclopramide group.

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References

1. CULVER GA, MAKEL HP, BEECHER HK. Frequency of aspiration of gastric contents by the lungs during anesthesia and surgery. *Annals of Surgery* 1951; **133**: 289-93.
2. BERSON W, ADRIANI J. 'Silent' regurgitation and aspiration during anesthesia. *Anesthesiology* 1954; **15**: 644-9.
3. BLITT CD, GUTMAN HL, COHEN DD, WEISMAN H, DILLON JB. 'Silent' regurgitation and aspiration during general anesthesia. *Anesthesia and Analgesia* 1970; **49**: 707-12.
4. TURNDORF H, RODIS ID, CLARK TS. 'Silent' regurgitation during general anesthesia. *Anesthesia and Analgesia* 1974; **53**: 700-3.
5. DUFFY BL. Regurgitation during pelvic laparoscopy. *British Journal of Anaesthesia* 1979; **51**: 1089-90.
6. CARLSSON C, ISLANDER G. Silent gastropharyngeal regurgitation during anesthesia. *Anesthesia and Analgesia* 1981; **60**: 655-7.
7. FASANO M, KOFKE WA, KEAMY MF. Continuous hypopharyngeal pH during mask anesthesia. *Anesthesiology* 1986; **65**: A172.
8. ONG BY, PALAHNIUK RJ, CUMMING M. Gastric volume and pH in out-patients. *Canadian Anaesthetists' Society Journal* 1978; **25**: 36-9.
9. THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN. *Martindale, the extra pharmacopoeia*, 28th edn. London: The Pharmaceutical Press, 1982: 426.
10. CLARK JM, SEAGER SJ. Gastric emptying following premedication with glycopyrrrolate or atropine. *British Journal of Anaesthesia* 1983; **55**: 1195-9.
11. BROCK-UTNE JG, DOW TGB, DIMOPOULOS GE, WELMAN S, DOWNING JW, MOSHAL MG. Gastric and lower oesophageal sphincter (LOS) pressures in early pregnancy. *British Journal of Anaesthesia* 1981; **53**: 381-4.
12. TODD JG, NIMMO WS. Effect of premedication on drug absorption and gastric emptying. *British Journal of Anaesthesia* 1983; **55**: 1189-93.
13. HALL AW, MOOSSA AR, CLARK J, COOLEY GR, SKINNER DB.

- The effects of premedication drugs on the lower oesophageal high pressure zone and reflux status of Rhesus monkeys and man. *Gut* 1975; 16: 347-52.
14. HEY VMF, OSTICK DG, MAZUMDER JK, LORD, WD. Pethidine, metoclopramide and the gastro-oesophageal sphincter. A study in healthy volunteers. *Anaesthesia* 1981; 36: 173-6.
 15. BROCK-UTNE JG, RUBIN J, WELMAN S, DIMOPOULOS GE, MOSHAL MG, DOWNING JW. The action of commonly used antiemetics on the lower oesophageal sphincter. *British Journal of Anaesthesia* 1978; 50: 295-8.
 16. BROCK-UTNE JG, RUBIN J, DOWNING JW, DIMOPOULOS GE, MOSHAL MG, NAICKER M. The administration of metoclopramide with atropine. *Anaesthesia* 1976; 31: 1186-90.
 17. O'MULLANE EJ. Vomiting and regurgitation during anaesthesia. *Lancet* 1954; 1: 1209-12.
 18. COTTON BR, SMITH G, FELL D. Effect of oral diazepam on lower oesophageal sphincter pressure. *British Journal of Anaesthesia* 1981; 53: 1147-9.
 19. RUBIN J, BROCK-UTNE JG, DIMOPOULOS GE, DOWNING JW, MOSHAL MG. Flunitrazepam increases and diazepam decreases the lower oesophageal sphincter tone when administered intravenously. *Anaesthesia and Intensive Care* 1982; 10: 130-2.
 20. MADEJ TH, SIMPSON KH. Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following gynaecological surgery in day cases. *British Journal of Anaesthesia* 1986; 58: 879-83.

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Blood flow in the upper limb during brachial plexus anaesthesia

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Summary

Changes in finger blood flow, arm blood flow and cardiac output were measured using electrical impedance plethysmography in 20 patients after brachial plexus anaesthesia. The anaesthetic solution used in all patients was 1% lignocaine with adrenaline 1:200 000. Significant increases in cardiac output and blood flow to the unanaesthetised arm were observed immediately after anaesthesia had become effective. A highly significant increase in the blood flow to fingers of the blocked hand was observed throughout the period of anaesthesia but there was no overall increase in the blood flow to the arm. It is suggested that the adrenaline contained in the local anaesthetic solution increased the cardiac output and caused arterial vasoconstriction at the site of injection.

Key words

*Anaesthetic techniques, regional; brachial plexus.
Measurement techniques; impedance plethysmography.*

Brachial plexus anaesthesia provides excellent operative conditions for arm and hand surgery. The block interrupts the sympathetic nervous supply of the upper limb in addition to the production of surgical anaesthesia, and may result in increases in the arterial blood flow and venous capacity of the upper limb. An increase in arm blood flow is thought to be an advantage in microvascular and re-implantation surgery, since it may improve the chance of survival of marginally viable skin flaps and may increase the patency rate of microvascular arterial anastomoses. Continuous brachial plexus anaesthesia has been described as a therapeutic method to increase arm and finger blood flow in re-implantation surgery.^{1,2}

Previous work demonstrated an increase in arm blood flow after brachial plexus anaesthesia; the increase was significantly greater when the anaesthetic solution contained adrenaline.³ However, no measurements of cardiac output were made during this study and the duration of blood flow changes was not investigated, except for one isolated

measurement which suggested an increase in blood flow 24 hours after surgery.

In the present investigation changes in the cardiac output, blood flow in both arms and blood flow in one finger of each hand were investigated following brachial plexus anaesthesia. The measurements were continued until the anaesthetic effects of the block were no longer apparent. The blood flow changes were measured by electrical impedance plethysmography, a technique which has been used widely for the measurement of cardiac output^{4,5} and has been adapted for the measurement of blood flow in the arm⁶ and fingers.⁷ The method of measurement is non-invasive and causes little discomfort to the patient.

Methods

The study was undertaken on 20 patients who underwent elective or emergency hand surgery. Informed consent was obtained from the patients and the experimental protocol

Table 1. Details of patients studied.

Age (years)	Sex	Reason for operation	Duration of anaesthesia (minutes)	Additional nerve blocks
<i>Axillary blocks</i>				
62	F	R thumb web division	370	
31	M	Amputation L little finger	310	
56	M	Tendon repair L thumb	270	Lateral cutaneous nerve block
57	M	L Dupuytren's contracture	270	
25	M	Nerve repair R index finger	350	Lateral cutaneous nerve block
21	M	Tendon repair L little finger	310	Ulnar nerve block
68	M	R Dupuytren's contracture	230	
73	F	R Dupuytren's contracture	380	Median nerve block
72	F	R Dupuytren's contracture	—	Failed block
68	M	Arthroplasty R thumb	—	Failed block
<i>Supraclavicular blocks</i>				
57	F	L carpal tunnel release	290	
38	M	Tendon repair R index finger	290	
23	M	Repair cut R thumb	300	
29	M	R 5th metacarpal fracture	290	
69	M	Removal R trapezium	250	
21	M	Crush injury R index finger	200	
49	M	Removal granuloma L hand	340	
46	M	Tendon repair R index finger	210	Local infiltration
65	M	Amputation R little finger	300	Median + ulnar nerve block
16	M	Crush injury	—	Failed block

had the approval of the hospital ethical committee. Patients received either an axillary or a supraclavicular brachial plexus block (Table 1). Anxious patients received oral lorazepam 2 mg and metoclopramide 10 mg as premedication, and increments of intravenous midazolam to a maximum of 10 mg were administered to provide sedation as necessary during surgery.

The local anaesthetic used in all cases was lignocaine 1% with adrenaline 1:200 000. The total dose of lignocaine did not exceed a maximum of 6 mg/kg. The supraclavicular blocks were performed by a modified Patrick's technique; an attempt was made to elicit paraesthesia prior to the injection of 30–35 ml of local anaesthetic solution. The axillary blocks were performed by a two-needle technique using 35–40 ml of local anaesthetic solution, without the use of a tourniquet to limit distal spread. An additional peripheral nerve block was given at the elbow or wrist if anaesthesia was incomplete after 20 minutes. The technique was judged to have failed if there was no analgesia after 30 minutes, and surgery was then completed under general anaesthesia.

Cardiac output measurements were taken from a segment of the thorax measured from the xiphoid process of the sternum to the base of the neck.⁴ Arm blood flow measurements were taken from a 15-cm segment of the arm centred on the elbow joint. Finger blood flow measurements were taken from a 1.5-cm length of the index, middle or ring finger, measured distally from the proximal interphalangeal joint. Values for cardiac output and arm and finger blood flows were calculated from the impedance waveform obtained during cardiac ejection and peripheral arterial pulsation, using the method of Kubicek.^{4,5}

Baseline measurements of cardiac output, arm blood flow and finger blood flow were made prior to the injection of local anaesthetic solution. The measurements were repeated as soon as surgical anaesthesia developed and again at the conclusion of the operation. Measurements were repeated on the ward at intervals of approximately 1 hour until the motor and analgesic effects of the block were no longer apparent. The surface temperature of the finger pulp was recorded using a skin probe and the motor and sensory effects of the block were assessed during each set of blood flow measurements.

The arm and finger blood flow results were analysed by two methods. All the cardiac output, arm blood flow, finger blood flow and temperature measurements recorded during the anaesthetic were compared with baseline values using the Wilcoxon matched-pairs test; individual readings were also compared to control readings taken simultaneously from the contralateral arm and finger. In addition, the arm and finger blood flow measurements were compared to a range of values collected previously from 142 normal individuals aged 17–88 years.^{6,8} The ranges of blood flow in the arm and finger were found to be wide and did not follow a Gaussian distribution. It was therefore difficult to establish a useful range of absolute values. However, a normal range was established for the ratio of the blood flow between opposite arms and fingers.⁸ The blood flow ratio is calculated by dividing the blood flow value in the right arm or in any finger of the right hand, by the corresponding blood flow value on the left side. The range for this ratio in normal subjects was found to be 0.66–1.5 in the arm and 0.5–2.0 in the middle three fingers.⁸ Values outside this range were considered to be abnormal.

The coefficient of variation of the cardiac output values was 10% in a study of 11 normal individuals at rest. The coefficient of variation was 16% for arm blood flow and 21% for finger blood flow in a similar study of 20 upper limbs.

Results

The results from three patients who required a general anaesthetic were not included in the study. The results from the other 17 patients were considered as a single group, since supraclavicular and axillary groups were indistinguishable.

A tourniquet was used in 16 of the 17 patients who received a complete block, with a mean duration of application of 32 minutes (range 8–64). The mean time between removal of the tourniquet and the first postoperative measurement was 34 minutes (range 12–111).

The baseline values for cardiac output, arm and finger blood flows and skin temperature are shown in Table 2. The pre-operative measurements taken immediately the block became effective, the postoperative measurements taken after the operation was completed and the final measure-

Table 2. Baseline measurements expressed as mean (SEM).

Cardiac output, ml/minute	6680 (610)
Blood flow, ml/minute	
Control arm	166 (15)
Blocked arm	200 (31)
Control finger	0.20(0.02)
Blocked finger	0.24(0.01)
Temperature, °C	
Control finger	27.8(0.7)
Blocked finger	27.8(0.6)

Table 3. Changes from baseline values of cardiac output, arm and finger blood flows (ml/minute) and finger temperatures (°C) expressed as mean (SEM). See text for details of measurement times. Blood flow values are also expressed as mean percentage change from baseline [in brackets].

	Pre-operative	Postoperative	Final
Cardiac output	1096 (357) [20%]**	-500 (350) [-7%]	-480 (357) [-7%]
Blood flow			
Control arm	36.5 (12.1) [28%]**	4.5 (13.3) [7%]	-21.6 (12.5) [-17%]
Blocked arm	17.7 (32.6) [2%]	-22.6 (19.0) [-11%]	-10.3 (32.9) [-9%]
Control finger	0.12 (0.03) [83%]**	0.12 (0.04) [93%]**	0.16 (0.04) [104%]**
Blocked finger	0.43 (0.13) [249%]***	0.48 (0.07) [348%]***	0.19 (0.05) [137%]**
Temperature			
Control finger	1.16 (0.76)	3.25 (0.94) **	3.44 (0.88) **
Blocked finger	4.81 (0.77) ***	4.75 (0.90) ***	2.66 (0.93) *

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

ments taken when the clinical effects of the anaesthetic were no longer apparent, are shown in Table 3 as the absolute and percentage changes from baseline values.

Cardiac output increased significantly immediately after the anaesthetic took effect; cardiac output values after surgery and at the final reading were close to baseline. Blood flow in the unanaesthetised control arm increased significantly immediately after the anaesthetic took effect but there were no significant changes in blood flow in the anaesthetised arm at any time during the study, when compared to baseline values. Finger blood flow measurements in both hands increased significantly above baseline after administration of the block. The increases in blood flow in the anaesthetised fingers were significantly greater ($p < 0.001$) than the changes in the control fingers at both the pre- and postoperative readings. Blood flows in both hands at the final reading, were significantly greater ($p < 0.01$) than the baseline values. There was a small but insignificant reduction in flow to the blocked arm following brachial plexus anaesthetic (Table 4). In contrast, there was a highly significant increase in finger blood flow.

The numbers of patients with a blood flow ratio above or below the normal range are shown in Table 5. Significantly increased arm blood flow ratios were observed in five patients before anaesthesia. Finger blood flow ratios

Table 4. Differences between arm or finger blood flows in anaesthetised and control arms expressed as a percentage of the control value at the four measurement times.

Blood flow	Baseline	Pre-operative	Post-operative	Final
Arm	14%	-13%	-17%	34%
Finger	29%*	130%***	140%***	28%

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 5. Numbers of patients whose arm or finger blood flow ratios (anaesthetised:control) were outside normal limits.

Blood flow ratio	Baseline	Pre-operative	Post-operative	Final
Arm				
High	5	3	3	2
Low	2	6	2	0
Finger				
High	1	9	10	3
Low	1	0	0	1

exceeded the normal range in 10 patients during brachial plexus anaesthesia. Immediately after successful brachial plexus anaesthesia, four patients who had a normal arm blood flow ratio at the baseline reading were found to have a reduction of blood flow in the blocked arm, which reduced the ratio to below the normal range. The observation of individuals with blood flow ratios outside the normal range at the baseline reading, is accounted for by the patients' injury or pre-existing surgical condition.

The skin temperatures of both the anaesthetised and control hands increased after the anaesthetic was administered (Table 3). Both hands remained significantly warmer at the final reading than at the start of the study but the control fingers were warmer than those on the side which had undergone surgery.

Discussion

The results of the present investigation show an increase in finger blood flow in the blocked hand throughout the period of the anaesthetic. There were also increases in cardiac output and in blood flow to the unanaesthetised arm immediately after administration of the block.

The increase in cardiac output was due a rise in heart rate rather than an increase in stroke volume. This effect was observed after the administration of the block and is probably due to absorption of adrenaline from the site of injection. Apprehension on the part of the patient may be an additional factor but a significant increase in cardiac output from anxiety might be expected before anaesthesia rather than after performance of the block. An increase of 30% in cardiac output was reported after administration of local anaesthetic solutions that contained 1:200 000 adrenaline into the epidural space.⁹

The increase in blood flow to the control arms after insertion of the block and the subsequent return to baseline values during the postoperative period, paralleled the changes in cardiac output. The percentage changes of both measurements were similar, which suggests that the changes in the control arm blood flow may be secondary to alterations in cardiac output.

In contrast, the blood flow to the blocked arms did not change after the anaesthetic, although some patients demonstrated a marked increase whilst others showed a small decrease. The flow was nearly double the baseline value in two of the patients in whom blood flow increased.

The observation that the blood flow in some of the blocked arms was reduced despite the increase in cardiac output after the anaesthetic, suggests that arterial vasoconstriction may have limited the blood flow. Vasoconstriction might possibly be due to the direct effect of pressure on the artery or to irritation caused by the injection of a large volume of local anaesthetic solution, but the adrenaline must be assumed to be the most important aetiological factor.³ The area of contact between the artery and the local anaesthetic solution varies in each patient and is determined to a major extent by the anatomy of the fascial compartments that enclose the brachial plexus. Adrenaline

would be expected to produce intense and prolonged vasospasm when it does come into contact with the vessels.

Increases in blood flow secondary to tourniquet-induced hyperaemia were not observed in this study. Changes may have taken place but they may have been missed due to the lapse of time (average 34 minutes) between tourniquet release and the first postoperative reading. Hyperaemic changes may have influenced the blood flow measurements at the postoperative reading although further increases in flow would not have been possible if the vessels were already fully dilated due to the sympathetic block.

The temperature of the control hands was not constant throughout the study and some warming was observed. This gradual increase in temperature would account for the modest increase in blood flow in the fingers of the control hand during the study. The highly significant temperature increase in the fingers of the blocked hand probably reflects the action of the sympathetic blockade, which removes normal vasomotor tone and causes an increase in blood flow. The lower temperature of both hands at the start of the study may reflect a journey to the operating theatre along cold corridors. The temperature difference between the two hands at the final reading may be accounted for by the need to elevate and partly to expose the operated limb.

The results of the present investigation contrast with those of a previous study by McGregor *et al.*³ in which the arm blood flow was found to increase significantly after brachial plexus anaesthesia. Several differences exist between the present study and that of McGregor. The methods of blood flow measurement were different. The previous study used a Whitney strain gauge¹⁰ placed around the most muscular part of the forearm and used the principle of venous occlusion plethysmography. Impedance plethysmography measures the pulsatile blood flow in a segment of finger or arm and does not require the venous capacity, which is increased during sympathetic block, to become full and distended in order to record the measurements. In addition, the sites of arm blood flow measurement were different in the two studies. McGregor used a more distal site, where the effects of axillary artery vasoconstriction may have been less apparent. The anaesthetic solution used in the previous study was a mixture of bupivacaine 0.5% and lignocaine 1.5% which contained 1:100 000 adrenaline, double the concentration used in the present investigation. Adrenaline in higher concentrations may have a greater effect in increasing cardiac output, which in turn might offset any reduction in flow caused by arterial vasoconstriction.

The results of this study suggest that brachial plexus anaesthesia changes the pattern and distribution of blood flow in the limb. It appears that the blood flow to the fingers increases, irrespective of any changes that take place in total arm blood flow. The theory that redistribution of blood occurs during brachial plexus anaesthesia is supported by evidence of sympathectomy in the lower limb, where reduction in sympathetic tone may selectively promote blood flow to the skin and the digital arteries at the expense of blood flow to the other structures such as muscle and bone.¹¹

The addition of adrenaline to local anaesthetic solutions to prolong the period of brachial plexus anaesthesia may need to be questioned in some circumstances. The use of a solution that contains adrenaline would appear to have an unpredictable effect if the total blood supply to the limb is

to be increased, and in some cases may lead to a reduction in blood flow. This is not desirable if the circulation is already compromised or if the intention of brachial plexus anaesthesia is to increase blood flow. The results of this study suggest that solutions which contain adrenaline should be avoided if it is important not to decrease the overall blood supply to the limb.

Conclusions

The changes in upper limb blood flow that result from brachial plexus anaesthesia do not outlast the clinical anaesthetic effects of the block. The addition of adrenaline to the local anaesthetic solution may not increase the total limb flow but does increase blood flow to the distal part of the limb.

Acknowledgments

We are grateful to the consultant surgeons of the Wessex Centre for Plastic Surgery and Maxillo-Facial surgery and to the Consultant Anaesthetists of Odstock Hospital for permission to study their patients. We thank Dr P.G. Shakespeare for statistical advice and help with the manuscript. We are also grateful to the recovery nurses of Odstock Hospital for their cooperation and to the Medical Physics Department of the Royal United Hospital, Bath for the loan of the plethysmograph.

References

1. BERGER A, TIZIAN C, ZENZ M. Continuous plexus blockade for improved circulation in microvascular surgery. *Annals of Plastic Surgery* 1985; **14**: 16–19.
2. MATSUDA M, KATO N, HOSOI M. Continuous brachial plexus block for replantation in the upper extremity. *Hand* 1982; **14**: 129–34.
3. MCGREGOR AD, JONES WK, PERLMAN D. Blood flow in the arm under brachial plexus anaesthesia. *Journal of Hand Surgery* 1985; **10**: 21–4.
4. KUBICEK WG, KOTTKE FJ, RAMOS MH, PATTERSON RP, WITSOE DA, LABREE JW, REMOLE W, LAYMAN TE, SCHOENING H, GARAMELLA JT. The Minnesota impedance cardiograph—theory and applications. *Biomedical Engineering* 1974; **9**: 410–6.
5. PORTER JM, SWAIN ID. The measurement of cardiac output by electrical impedance plethysmography. *Journal of Biomedical Engineering* 1987; **9**: 222–31.
6. PORTER JM, SWAIN ID, SHAKESPEARE PJ. Measurement of limb blood flow by electrical impedance plethysmography. *Annals of the Royal College of Surgeons of England* 1985; **67**: 169–72.
7. MONTGOMERY LD. Comparison of an impedance device to a displacement plethysmograph for study of finger blood flow. *Aviation, Space and Environmental Medicine* 1976; **47**: 33–8.
8. PORTER JM, SWAIN ID, SHAKESPEARE PJ. The measurement of pulsatile limb and finger blood flow by electrical impedance plethysmography: criteria for the diagnosis of abnormal flow. *Journal of Biomedical Engineering* 1987; **9**: 367–73.
9. WARD RJ, BONICA JJ, FREUND FG, AKAMATSU T, DANZIGER F, ENGLESON S. Epidural and subarachnoid anesthesia. Cardiovascular and respiratory effects. *Journal of the American Medical Association* 1965; **191**: 275–8.
10. WHITNEY RJ. The measurement of volume changes in human limbs. *Journal of Physiology* 1953; **121**: 1–27.
11. COUSINS MJ, REEVE TS, GLYNN CJ, WALSH JA, CHERRY DA. Neurolytic lumbar sympathetic blockade: duration of denervation and relief of rest pain. *Anaesthesia and Intensive Care* 1979; **7**: 121–35.

Enhanced brachial plexus blockade. Effect of pain and muscular exercises on the efficiency of brachial plexus blockade

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Summary

Three groups each of 20 patients scheduled to undergo operations on hand or forearm, received supraclavicular brachial plexus blocks with 25 ml lignocaine 1.5%. Patients in the control group did not suffer from pain and were not asked to do muscular exercise. Patients with acute trauma of the upper limb formed the pain group and showed significantly decreased latency for onset of analgesia, partial and complete muscle paralysis. Patients in the muscle exercise group were free of pain and were asked to do muscular exercise for 5 minutes after injection of the lignocaine. Onset of analgesia, partial and complete muscle paralysis was significantly more rapid than in both control and pain groups. Changes in the duration of block were not significant. It is concluded that pain and muscular exercise enhance the onset of brachial plexus blockade.

Key words

Anaesthetic techniques, regional; brachial plexus block.

Regional nerve block of the upper limb is a useful and safe anaesthetic technique. Most upper limb surgery is for trauma and hence of a relatively urgent nature with little time to prepare the patient adequately.¹ Brachial plexus blockade provides ideal operating conditions for the surgeon with good analgesia and complete muscular relaxation, and sympathetic block which reduces post-operative vasospasm, pain and oedema.^{1,2}

One of the disadvantages of brachial plexus block is the latency of onset, which may be as long as 30 minutes.³ It has been postulated that high frequency nerve impulses increase anaesthetic effectiveness,⁴ and hence this study was designed to investigate the effect of pain and muscle exercise in enhancing the onset of analgesia and motor block after brachial plexus blockade.

Methods

The study was carried on 60 adult patients who were to undergo a variety of operations that involved the hand or forearm. The patients were generally healthy, as confirmed by clinical examination and routine laboratory investigations. They were classified into three groups, each of 20 patients: a control group of 17 males and 3 females, aged 17-40 years (mean 26.7 years) who were pain free and scheduled to undergo elective operations (Table 1) and who were not asked to do hand exercises after injection of local anaesthetic; a muscular exercise group of 10 males and 10 females, aged 17-45 years (mean 24.5 years), also pain free and to undergo elective operations (Table 1), who were asked to do repetitive, quick and forcible hand exercises (opening and closing) for 5 minutes immediately after injection of the local anaesthetic; and a pain group that included 14 males and 6 females, aged 20-40 years (mean 28.4 years) who suffered from pain as a result of acute

Table 1. Types of operation in control and muscle exercise groups (painless lesions).

Operation	Number
Plate extraction	9
Tendon graft	6
Z-plasty of contracted scar	7
Dorsal ganglion excision	10
Tendon sheath slitting	6
Osteotomy	2
Total	40

Table 2. Types of operation in pain group (painful lesions).

Operation	Number
Reduction forearm fracture, both bones	6
Reduction of Colles' fracture	9
Reduction of Smith's fracture	3
Repair of crush injury of the hand	2
Total	20

hand or forearm trauma (Table 2). They were not asked to do hand exercises.

The 40 patients in the control and muscular exercise groups were selected alternately. None of the patients was aware of the nature of the study except for the routine consent to anaesthesia and surgery. All blocks were done by a single senior anaesthetist. Assessment of analgesia and muscle paralysis was carried out by another single trained anaesthetist who was unaware of the nature of the study.

No premedication was given. Supraclavicular brachial plexus blockade was performed using 25 ml lignocaine 1.5% as described by Wise.⁵ Patients in whom the block

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was unsuccessful within 30 minutes were not included in the study.

The following observations were recorded for all patients: onset of analgesia calculated as the time in minutes from commencement of local anaesthetic injection until cutaneous analgesia to pinprick was established in the entire hand and forearm;⁶ onset of motor paralysis calculated as the time in minutes from injection until the patient could no longer reach the pre-block pressure by compressing the cuff using the compressing cuff technique;⁷ complete motor paralysis, the time in minutes from injection until the patient was no longer able to produce any pressure on the cuff; and duration of analgesia, the time in minutes between establishment of analgesia and the first appearance of pinprick sensation at any point below the elbow.⁶

Means and standard deviations were calculated for all observations. The unpaired *t*-test was used to test the significance of changes between the control and each of the pain and muscular exercise groups.

Results

Onset of analgesia in the control group was after 14.25 minutes (SD 1.18) and the onset of motor paralysis was at 19.9 minutes (SD 1.09), while complete paralysis was recorded after 25.85 minutes (SD 1.65); analgesia lasted for 121.5 minutes (SD 15.66) (Table 3).

Table 3. Onset time and duration of brachial plexus block in the studied groups. Values expressed as mean (SD).

	Control	Pain	Exercise
Onset of analgesia, minutes	14.25 (1.18)	9.05* (1.16)	5.65**† (2.73)
Onset of motor paralysis, minutes	19.9 (1.09)	11.8* (1.08)	10.1*‡ (3.52)
Complete motor paralysis, minutes	25.85 (1.65)	16.3* (1.55)	13.0*† (4.3)
Duration of analgesia, minutes	121.5 (15.66)	117.7 (17.92)	123.0 (16.84)

* *p* < 0.001 compared to control group.
† *p* < 0.001, ‡ *p* < 0.05 compared to pain group.

Onset of analgesia in the pain group was after 9.05 minutes (SD 1.16), which was significantly shorter in comparison to the control group (*p* < 0.001). Onset of motor paralysis was after 11.8 minutes (SD 1.08), significantly quicker than in the control group (*p* < 0.001). Complete muscle paralysis was reached 16.3 minutes (SD 1.55) after injection, and again this was significantly less than in the control group (*p* < 0.001). The duration of analgesia was 117.7 minutes (SD 17.92).

Onset of analgesia in the muscular exercise group was after 5.65 minutes (SD 2.73), significantly shorter than in both the control and pain groups (*p* < 0.001). The onset of complete paralysis, at 10.1 minutes (SD 3.52), was significantly shorter than both control (*p* < 0.001) and pain groups (*p* < 0.05). Complete muscle paralysis was achieved in 13 minutes (SD 4.3), again significantly less than the control (*p* < 0.001) and pain groups (*p* < 0.001). The duration of analgesia was 123 minutes (SD 16.84).

Discussion

Brachial plexus blockade is one of the most useful and effective anaesthetic techniques for surgery on the upper extremities but its major disadvantage is the latency in producing an effective block. This was evident in the control group of this study, where the mean onset time for analgesia

was 14.25 minutes and that for complete paralysis was 25.85 minutes. Bromage and Gertel⁶ used 50 ml lignocaine 1% with 1:200 000 adrenaline via the supraclavicular approach and recorded a latency time of 14.04 minutes (SD 3.83) for sensory blockade. Latency was reduced to 8.06 minutes (SD 2.94) when carbonated lignocaine was used. The improved effect is probably due to greater availability of free base. The addition of adrenaline 1:200 000 produces a more favourable block, shortens latency and increases the degree of blockade and the duration of analgesia. This improvement in the quality of blockade is associated with a diminished uptake of local anaesthetic into the circulation and an increased concentration around the nerves.⁸

In our study, onset of analgesia, motor block and time to complete block in the pain group was significantly more rapid by 36.5%, 40.7% and 36.9%, respectively, compared to the control group. Heffington and Thompson³ used 1.5% lignocaine with 1:200 000 adrenaline via the interscalene route for manipulative reduction of dislocation and fractures of upper extremities, and found the onset of analgesia to be almost immediate but that it may not be complete for at least 15 minutes.

Patients in the muscle exercise group showed the most rapid onset of analgesia, motor paralysis and complete motor paralysis. The latency was shorter by 60.4%, 49.2% and 49.7%, respectively, compared to the control group.

Nociception is a frequency encountered phenomenon. The intensity of pain increases with increased stimulation frequency, once threshold is reached. Noxious stimuli must have mid to high frequency conduction to be interpreted as painful. Motor function, on the other hand, has no threshold; it can be effective at low frequency, because a single impulse can cause a contraction and because many, if not all muscles are innervated plurineurally.

Charged or hydrophilic local anaesthetics with low lipid solubility such as lignocaine or bupivacaine show strong frequency effects. They reach the receptor primarily through the open sodium channel and bind more strongly to the closed than to the open conformation.⁹ Thus the effects of these drugs are highly related to repetitive firing, because the sodium channel opens and closes with each impulse; this accounts for the observed phenomenon of use-dependent anaesthetic block or frequency-dependent conduction block.^{4,10} The rapid onset of analgesia in the pain and muscle exercise groups can be explained on this basis, as due to the high stimulation frequencies which open the sodium channels. The block is slow when the nerve is at rest and grows faster as the nerve is stimulated with a train of depolarising pulses, and reaches a new steady state of inhibition.

Repetitive muscle contraction was more effective in shortening latency than was pain. It enhanced sensory loss more than muscular paralysis. Muscle contraction induces repetitive firing through the nerves and may also help the spread of local anaesthetic solution through the brachial plexus sheath. It is a simpler, more effective, harmless manoeuvre and adds no extra cost to the patient when compared with other techniques used to enhance the onset of local anaesthetic action, such as carbonation of the local anaesthetic or the addition of vasopressors.

References

1. DE JONG RH. Axillary block of the brachial plexus. *Anesthesiology* 1961; **22**: 215-25.
2. LA GRANGE PP, FOSTER PA, PRETORIUS LK. Application of the Doppler ultrasound bloodflow detector in supraclavicular brachial plexus block. *British Journal of Anaesthesia* 1978; **50**: 965-7.
3. HEFFINGTON CA, THOMPSON RC. The use of interscalene block anaesthesia for manipulative reduction of fractures and dis-

- locations of the upper extremities *Journal of Bone and Joint Surgery* 1973; **55A**: 83–6.
4. STRICHARTZ GR. Physiology of nerve transmission (including comments on the mechanisms of local anesthetic action). *Seminars in Anaesthesia* 1983; **2**: 1–9.
 5. WISE RP. Pain clinic and operative nerve blocks. In: CHURCHILL-DAVIDSON HC, ed. *A practice of anaesthesia*. London: Lloyd Luke, 1984: 893–935.
 6. BROMAGE PR, GERTEL M. An evaluation of two new local anaesthetics for major conduction blockade. *Canadian Anaesthetists' Society Journal* 1970; **17**: 557–64.
 7. WINNIE AP, LA VALLEE DA, PE SOSSA B, MASUD KZ. Clinical pharmacokinetics of local anaesthetics. *Canadian Anaesthetists' Society Journal* 1977; **24**: 252–62.
 8. BROMAGE PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1965; **16**: 55–69.
 9. SCURLOCK JE, MEYMARIS E, GREGUS J. The clinical character of local anaesthetics: a function of frequency-dependent conduction block. *Acta Anaesthesiologica Scandinavica* 1978; **22**: 601–8.
 10. COURTNEY KR, KENDIG JJ, COHEN EN. Frequency-dependent conduction block: the role of nerve impulse pattern in local anesthetic potency. *Anesthesiology* 1978; **48**: 111–7.

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Micro-aggregates and filtration

The last few years have seen changes in the way blood is packaged. It is now presented to the users, often anaesthetists, in glass bottles or plastic packs and from acid-citrate-dextrose to Optimal Additive Solutions (OAS). One example is the Fenwal OAS, otherwise known as Saline Adenine Glucose Mannitol (SAGM) blood, which is also widely distributed in Holland with, in most cases, the advice that micro-aggregate filtration is not necessary. In this hospital the cardiac unit is the only place where filtration is applied routinely.

Recently large lumps of debris have been visible in the empty bags after transfusion or trapped in the giving set filter. The blood bank was contacted and stated that this problem might originate with the collection technique. The large aggregates were seen repeatedly and so it was decided to institute a simple study to assess the incidence of visible particulate matter in the Fenwal OAS blood.

For 4 weeks all the blood delivered to the cardiac operation rooms was non-invasively examined by two observers who worked independently. The dates of collection and examination allowed the blood age to be calculated; each bag was scrutinised against background light and gently compressed to produce a thin film. The blood was allowed to flow through the examination area and the presence of particles graded as 0 for none seen, 1 if present but < 2 mm, and 2 if > 2 mm.

Three hundred and twenty-one units of blood were examined in all, the majority of which were less than 10 days old and visible macro-aggregates, thus greater than 40 microns, were present in 45.5% of the bags. There was absolute agreement between the observers in 70% of cases; 40% of the disagreement was between grades 1 and 2. The

Age (days)	Grades		
	0	1	2
0-5	109	19	18
6-10	62	33	54
11-15	3	4	12
16-20	1	1	5

relationship between age and aggregates is set out in the table.

The cardiac unit is fortunate in that it receives relatively recently given blood but even the blood less than 5 days old is not completely free from macro-aggregates, the numbers of which can only be guessed. The frequency of macro-aggregates in our survey was less than the 85% found by Robertson *et al.*¹ but this can be explained, not on regional or national boundaries but by the technique used; we had to preserve the integrity of the package for later use and so could easily have missed some isolated clumps in otherwise clear blood.

Some blood distribution centres have propagated the message that filtration of the SAGM blood is not necessary. This advice may be inappropriate, with the present day evidence on the need to remove micro-aggregates, especially in view of the mass of particles that the blood apparently contains.¹ Micro-aggregates may have a role to play in the development of adult respiratory distress syndrome² but have also been shown to contribute to nonhaemolytic febrile reactions³ and to a reduction in platelet levels in certain patients.⁴

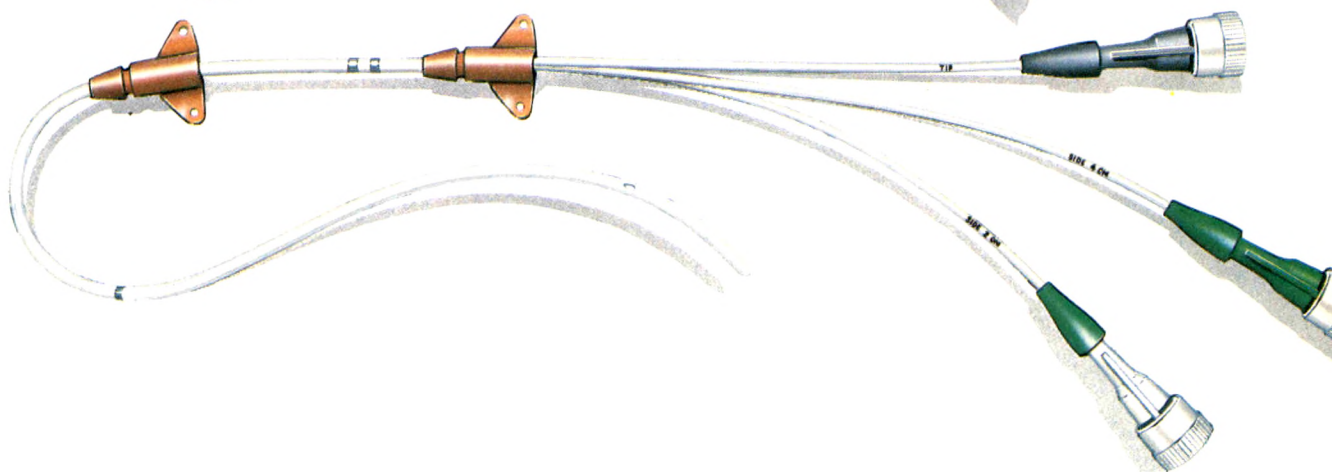
It would seem reasonable in the light of this and other

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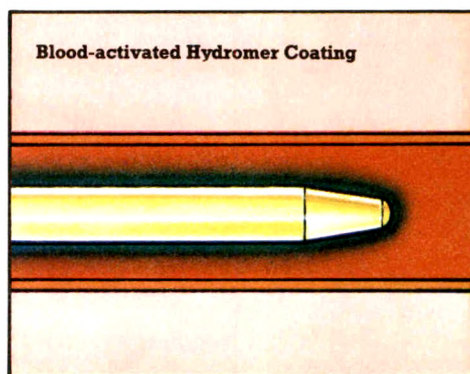
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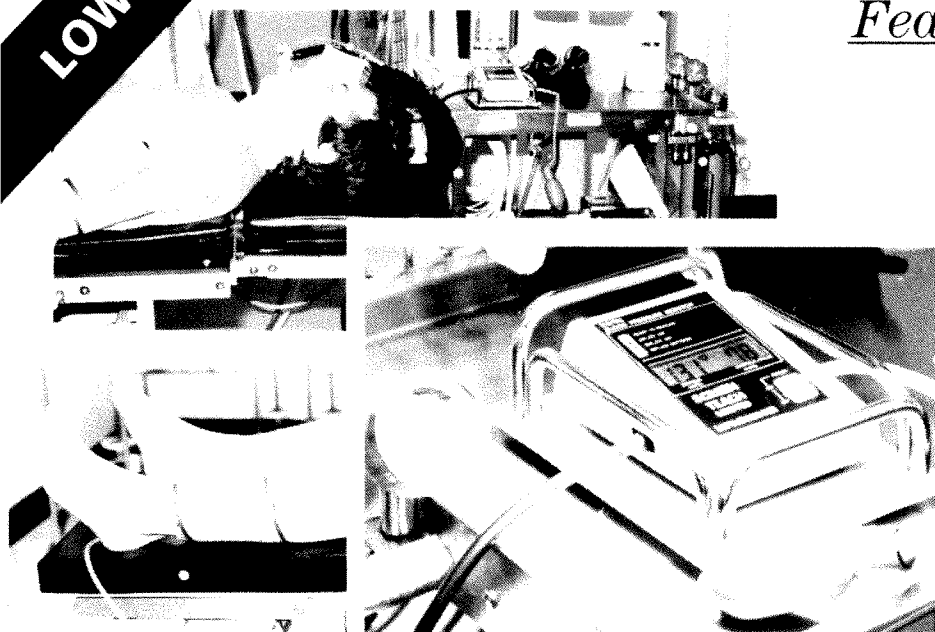
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work to repeat the words of Wenz⁵ 'A medical device which proves to have at least one advantage and no documented disadvantages is never superfluous' and to advise that all ages of the Fenwal OAS blood be filtered—advice which can probably be extended to all transfused blood.

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References

1. ROBERTSON M, BOULTON FE, DOUGHTY R, MACLENNAN JR, COLLINS A, MCCLELLAND DBL, PROWSE CV. Macro-aggregate formation in optimal additive red cells. *Vox Sanguinis* 1985; 49: 259–66.
2. REUL GJ JR, BEALL AC JR, GREENBERG SD. Protection of the pulmonary microvasculature by fine screen blood filtration. *Chest* 1974; 66: 4–9.
3. MERYMAN HT, HORNBLLOWER H. The preparation of red cells depleted of leukocytes. Review and evaluation. *Transfusion* 1986; 26: 101–6.
4. BAREFORD D, CHANDLER S, HAWKER R, JACKSON N, SMITH M, BOUGHTON B. Thrombocytopenia after routine blood transfusion: the response to filtered/washed blood products and the role of splenic sequestration. *British Journal of Haematology* 1987; 66: 574.
5. WENZ B. When is the microfiltration of whole blood and red cell concentrates essential? When is it superfluous? International Forum. *Vox Sanguinis* 1986; 50: 63–4.

Continuous infusion of propofol

We would like to report the following case history in view of the guarded interest shown in the continuous infusion of propofol for sedation in intensive care.^{1,2}

A thirty-one-year-old male demolition worker suffered fractured ribs, tibia and lumbar spine, after a ceiling collapsed on him. Four days after admission he developed confusion and respiratory failure and was treated with intermittent positive pressure ventilation (IPPV) of the lungs on the ICU. Arterial blood analysis on admission showed P_{aO_2} 7.0 kPa on F_{iO_2} 0.6. Pulmonary artery catheterisation revealed normal wedge pressure with elevated pulmonary artery pressure. He steadily improved with standard care and prostacyclin infusion and was weaned from IPPV after 21 days. A propofol infusion was commenced at one stage because of difficulty with sedation and a decrease in dynamic lung compliance. This was maintained for 11 days at a level sufficient to maintain sleep (Ramsay Level 6).³ A vecuronium infusion was also used for a period of 5 days while the patient was severely hypoxic (P_{aO_2} 5–6 kPa F_{iO_2} 0.6, 0.5 kPa PEEP, reversed 1:E ratio) to prevent airway pressure peaks (peak airway pressures 4–5 kPa). He received a mean daily dose of 6.7 gm propofol (64 μ g/kg/minute) during this period. This compares with the Hammersmith¹ experience (13.3 μ g/kg/minute), Glasgow² (34 μ g/kg/minute) and Dundee⁴ (66 μ g/kg/minute). He received 46 gm of propofol, which cost about £1150, during the whole course of his treatment. Complications, possibly related to sedation, were severe episodes of bradycardia during movement or underventilation which made airway suction, pressure area care or tube changes hazardous. This problem may have been because of vecuronium infusion.⁵ One epi-

sode of green urine was noted as previously described by Bodenham *et al.*⁶ This was because of phenol metabolites of propofol and is not thought to be dangerous.

A Synacthen test taken shortly after the end of the infusion revealed normal adrenocortical function. The patient made an excellent recovery, is mentally quite normal and has no recollection of the period of IPPV.

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References

1. GROUNDS RM, LALOR JM, LUMLEY J, ROYSTON D, MORGAN M. Propofol infusion for sedation in the intensive care unit: preliminary report. *British Medical Journal* 1987; 294: 397–400.
2. NEWMAN LH, McDONALD JC, WALLACE PGM, LEDINGHAM IMCA. Propofol infusion for sedation in intensive care. *Anaesthesia* 1987; 42: 929–37.
3. RAMSAY MAE, SAVEGE TM, SIMPSON BRJ, GOODWIN R. Controlled sedation with alphaxalone-alphadalone. *British Medical Journal* 1974; 11: 656–9.
4. MACKENZIE N, GRANT IS. Propofol for intravenous sedation. *Anaesthesia* 1987; 42: 3–6.
5. COZANITIS DA, POUTTU J, ROSENBERG PH. Bradycardia associated with the use of vecuronium. A comparative study with pancuronium with and without glycopyrronium. *Anaesthesia* 1987; 42: 192–4.
6. BODENHAM A, CULANK LS, PARK GR. Propofol infusion and green urine. *Lancet* 1987; 2: 740.

Leaks in breathing systems

Hanning, Kruchek and Chunara (*Anaesthesia* 1987; 42: 1329–30) describe a potentially lethal leak from an anaesthetic machine after it was serviced. The authors are to be congratulated in their prompt action but it is disturbing that the routine checks performed by the manufacturer's engineer and the anaesthetists did not reveal such a sizeable leak.

The leakage described was indeed very significant; if the leak is assumed to be selective for oxygen, the F_{iO_2} value of 0.1 to 0.15 represents an oxygen leakage of 1620–1940 ml/minute from a total oxygen flow of 2500 ml/minute. We are thus surprised that such a leak was apparently insufficient to prevent the usual transient fall in the level of the Rotameter bobbins from occlusion of the common gas outlet (CGO).

We fully support the call for in-line oxygen analysers, whose importance in the system is critical—a fact long known but poorly publicised. Most oxygen analysers measure partial pressure of oxygen and compare this to 101 kPa to derive F_{iO_2} . If the analyser is placed downstream from a Manley Pulmovent it produces a true reading. However, if the analyser is upstream of the Manley at the CGO, the back pressure produced by this ventilator in the backbar apparently raises the P_{O_2} and hence indicates an erroneously high F_{iO_2} . If the analyser were in this position in the authors' machine the true F_{iO_2} may well have been even less than the values given.

In the absence of oxygen analysers occlusion of the CGO is a helpful but coarse test for leakage. The test described by Page¹ is qualitatively and to a degree quantitatively

more discriminating. The machine common gas outlet is connected to a pressure gauge (such as a blood pressure gauge), the oxygen Rotameter is slowly opened and adjusted to maintain a pressure of 16 kPa in the backbar. The oxygen flow is an indication of the leakage and more than 200–300 ml/minute is considered unacceptable. (This does not measure the absolute leak flow under working conditions.) The oxygen flow in the machine in question would probably have been in the order of litres/minute with this method. This test is sensitive, reliable, rapidly and simply performed with equipment that is readily available in the anaesthetic room and might usefully be added to the protocol for testing anaesthetic machines.

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Reference

1. PAGE J. Testing for leaks. *Anaesthesia* 1977; 32: 673.

Editor's note

There was a misprint in the final paragraph of Hanning's letter: the pressure in the backbar is increased by the Manley ventilator to between 12 and 15 kPa (not 120 and 150) and the test pressure should be 20 kPa.

Epidural infusions—shortage of infusion devices

Our experience of epidural infusions for mothers in labour is very favourable. We use plain bupivacaine 0.125% via a Vickers Treonic C30 syringe driver. The following regimen is used after a 3-ml test dose of bupivacaine 0.5% with adrenaline 1 in 200 000 and a 3-ml increment of bupivacaine 0.25%. When the cervix is 6 cm dilated the infusion rate is 6 ml/hour; between 6 and 8 cm it is 8 ml/hour and at 8–10 cm it is 10 ml/hour, with a maximum dose of 0.4 ml/kg/hour. This infusion rate is varied with increments according to the pain relief achieved with the aim of a comfortable mother who is still aware of the sensation of contraction. A simple problem of inadequate availability of syringe pumps arose, which prevented the service, despite the increased efficacy of epidural infusion techniques.

In the late 1960s a large number of drip-counting infusion pumps were bought to facilitate infusions of syntocinon; however induction and active management of labour have declined in popularity since and many of these pumps are now redundant. Our aim is to make use of these pumps and provide a valuable service.

Syntocinon infusions are controlled on our unit by Ivac

531 and Tekmar 751 drip-count infusion pumps. Therefore, conversion of infusions to drops per minute, and a suitable concentration of bupivacaine made up was all that was required. The bupivacaine was diluted in 100 ml bags of normal saline from which 20 ml was withdrawn, and 40 ml of plain bupivacaine 0.25% was added which made a total of 120 ml of 0.083% bupivacaine.

The equivalent regimen to that one described above is 3, 4 and 5 drops per minute using 20 drop/ml administration sets. This may be augmented with increments of 2 ml of 0.25% bupivacaine and by a maximum of 0.2 drops/kg/minute, according to patient requirement.

We hope this tactic may help other anaesthetists who have equipment shortages and who are thus unable to offer epidural infusions to their patients.

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D.J. SAPSFORD

C. HOWARD

Withdrawal of anaesthetic ether

We the undersigned are extremely disquieted at the sudden withdrawal of anaesthetic ether by May and Baker Ltd, who are not to renew their Product Licence.

We consider that di-ethyl ether has still a definite, albeit limited, place in anaesthetic practice, in particular in the management of infants who are to have direct laryngoscopy or bronchoscopy, where its lack of respiratory depression relative to the fluorinated hydrocarbons and ethers may render it the agent of choice in the hands of practitioners skilled and experienced in its use.

A second, and in some ways a more important point, is that the withdrawal of ether is indicative of a practice that now appears to be recurrent, of peremptory withdrawal of the supply of a valued drug without adequate consultation

with the anaesthetic profession at large. This happened with alphaxalone/alphadolone, with trichloroethylene and now with diethyl ether. Such unilateral decisions about what we may or may not use are not conducive to trustful relations between anaesthetists and pharmaceutical manufacturers and, we believe, are not in the best interests of the profession.

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Bradycardia during elevation of zygomatic fractures

It was fascinating to read the case report of Drs Shearer and Wenstone (*Anaesthesia* 1987; 42: 1207–8) since it was only 2 months since I had witnessed a similar but much more severe episode. My patient, who had been involved in an affray, not only fractured his left zygomatic arch but also had mediastinal emphysema. All symptoms had settled

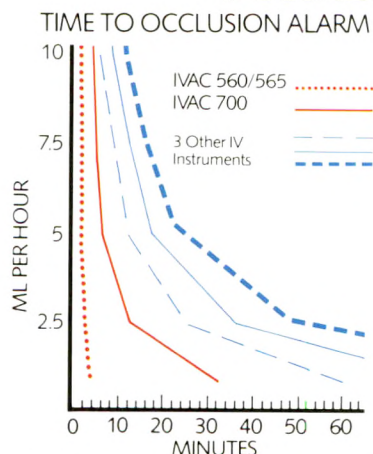
except that there was still an air shadow around the heart so nitrous oxide was avoided by the use of a drawover apparatus. The patient was premedicated with oral temazepam 20 mg and hyoscine 0.45 mg. He was brought to theatre and anaesthesia was induced with thiopentone 350 mg, and suxamethonium 100 mg was used to facilitate

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Hoechst UK Limited,
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tracheal intubation. Levorphanol 2 mg intramuscularly was given into the lateral aspect of the thigh and the patient breathed spontaneously oxygen-enriched air through an Oxford miniature vaporizer. The halothane concentration was reduced after induction from 4% to 2%; trichloroethylene was reduced from 0.5% to 0.2% and the patient was stable with a systolic blood pressure of 100 mmHg and a pulse of 75 per minute. There were two or three slow complexes and then two screens of a straight-line ECG when the zygomatic arch was elevated. External cardiac massage was started, during which time it was impossible to see the complexes on the ECG screen due to interference, and atropine 0.6 mg was given intravenously. The interference was stopped after 30 seconds of cardiac massage

and the pulse rate was found to have risen to 40 per minute. However, the blood pressure was again 100 mmHg systolic so cardiac massage was stopped. The patient continued to breathe normally and the operation was then completed and the patient awoke normally in recovery.

It is my practice to use an ECG during all operations but I have not noticed bradycardia during elevation of zygomatic arches in the past. However, I would support the suggestion of Drs Shearer and Wenstone that atropine should always be at hand during this procedure.

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Diclofenac

We were interested to read the paper by Hodsman *et al.* (*Anaesthesia* 1987; 42: 1005-8) and were impressed by the marked morphine-sparing effect demonstrated in Fig 1. One of the main determinants of postoperative pain is the site of the abdominal skin incision.¹ We are told little about the surgery apart from that it was corrective abdominal surgery. Were there comparable numbers of upper and lower abdominal incisions in both groups?

If the two groups were not comparable in this respect this would be an alternative explanation to the differences in the 4-hour pain scores.

groups studied are shown below. There was no difference between the two groups for operation sites and so we con-

	Gastric surgery	Cholecystectomy	Large bowel surgery
Diclofenac	10	13	8
Placebo	11	13	7

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sider that the reduction in pain scores at 4 hours was valid and was due to improved analgesia in those patients who received diclofenac.

Reference

1. LOAN WB, DUNDEE JW. The clinical assessment of pain. *Practitioner* 1967; 198: 759-68.

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A reply

Thank you for the opportunity to reply to the letter by Drs Goucke and Eadsforth. The type of operations for the two

Hazards of priming

We agree with Sosis (*Anaesthesia* 1988; 43: 249) that to prime is a technique which could result in serious complications. This is because of the variability of response to a small dose of non-depolarising muscle relaxant even in healthy unpremedicated patients. Does priming really accelerate neuromuscular blockade? Brady *et al.* have recently shown that to prime with both vecuronium and atracurium does not accelerate the onset as compared with single-dose administration.¹ No complications were observed² in a recent report of priming technique using vecuronium for patients who had Caesarean section but the mean onset time of 3.5 minutes was extremely long and certainly unsuitable for rapid sequence induction.

The unsatisfactory nature of the priming technique and the associated complications has made us try other methods for rapid tracheal intubation. We have recently concluded a study with a variety of doses of vecuronium, 0.1, 0.2 0.3 and 0.4 mg/kg given as a bolus. The shortest mean onset time of 100 seconds with excellent conditions for intubation was achieved with 0.3 mg/kg dose.

We thank Sosis for drawing our attention to the pitfalls of the studies on which our clinical trial was based.^{3,4}

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References

1. BRADY MM, MIRAKHUR RK, CLARKE RSJ, GIBSON FM. Administration of atracurium or vecuronium in divided doses does not accelerate their onset of action. *Anesthesiology* 1987; 67: A347.
2. TESSEM JH, JOHNSON TD, SKJONSBY BS, KUBICEK MF, JOYCE TH. Evaluation of vecuronium for rapid sequence induction in patients undergoing cesarean section. *Anesthesiology* 1987; 67: A452.
3. FOLDES F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs: the priming principle. *British Journal of Anaesthesia* 1984; 56: 663.
4. TABOADA JA, RUPP SM, MILLER RD. Refining the priming principle for vecuronium during rapid-sequence induction of anesthesia. *Anesthesiology* 1986; 64: 243-7.

Weak concentration of thiopentone

A 1% solution of thiopentone to induce anaesthesia in the elderly, rather than the 2.5% solution normally used, is in my opinion desirable. Davenport suggests 0.75% in saline.¹

The elderly need a smaller dose of intravenous induction agent, given much more slowly than in younger patients.^{2,3} The induction dose of thiopentone drops at the rate of 1 mg/kg for every decade,⁴ primarily because the initial distribution volume increases the time from injection to induction.⁵ It has been recommended that a small bolus should be given, and its effect watched for an appropriate time, say 30–60 seconds. The range recommended for the elderly is 1.26–2.45 mg/kg and the average time to loss of consciousness is 48 seconds (SD 2.4).

Dilution of thiopentone to 1% increases the safety of this technique. One can then titrate the effect of a dose better than with the normal low volume. An anaesthetist with little experience of the elderly would be much less likely to give an overdose; it is also easier to remember a concentration of 10 mg/kg and the use of a 5 or 10 ml syringe makes overdosage easier to avoid. 2.5% thiopentone has an osmolality (480–500 mosm/kg) higher than 1% in saline (370 mosm/kg) or 1% in water (188–195 mosm/kg); this should reduce local reactions if there is

extravasation which is far more likely with elderly, fragile veins. A 1% solution in water could however cause haemolysis.

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References

1. DAVENPORT HT. *Anaesthesia in the elderly*. London: Heinemann, 1986: p. 86.
2. DUNDEE JW. The influence of body weight, sex and age on the dosage of thiopentone. *British Journal of Anaesthesia* 1954; 26: 164–73.
3. CHRISTENSEN JH, ANDREASEN F, JANSEN JA. Influence of age and sex on the pharmacokinetics of thiopentone. *British Journal of Anaesthesia* 1981; 53: 1189–95.
4. HOMER TD, STANSKI DR. The effect of increasing age on thiopental disposition and anesthetic requirement. *Anesthesiology* 1985; 62: 714–24.
5. MURAVCHICK S. Effect of age and premedication on thiopental sleep dose. *Anesthesiology* 1984; 61: 333–6.

An unpredictable and possibly dangerous artefact affecting a pulse oximeter

A recent letter (*Anaesthesia* 1987; 42: 1116) reported several types of artefact from which a pulse oximeter derived apparently reasonable clinical values of Sao_2 and pulse rate. We agree with Dr Taylor's reply with regard to the value of the plethysmographic waveform, but there are also non-pulsatile sources of artefact which can lead to erroneous readings. The following example illustrates an artefact which will 'fool' the Biox 3700.

If some light-absorptive material such as a few thicknesses of semi-opaque or coloured plastic sheet is introduced into the light path of the finger, between the light emitting diodes and detection diodes, the Biox derives an Sao_2 of around 90–100% depending on thickness of the material. Furthermore, in the presence of normal room lighting a sinusoidal, pulse, waveform of frequency which varies between 20 and 70 bpm is often displayed *with no motion stimulus*

whatsoever. We cannot comment on the exact source of this spurious waveform but it may represent a beat frequency from the superimposition of room lighting upon some other cyclic signal within the instrument itself.

It is possible, although perhaps unlikely, that this effect may interfere with clinical measurements in a patient whose finger is small or not fully inserted in the probe.

The conclusion is obvious and need hardly be stated, any instrument is subject to interference from sources which are often unpredictable. Anaesthetists need to be as aware of the limitations of pulse oximetry as with all other instruments.

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Pain during injection of vecuronium

We have used vecuronium bromide to obtain during a clinical trial conditions for tracheal intubation rapidly and used the priming principle as previously described.¹ A number of patients complain of pain at the site of injection when a 23-G butterfly needle is used in the dorsum of the hand. Vecuronium bromide is reconstituted before use by dissolving buffered freeze-dried powder in sterile water for injection. The resultant acidity of the solution, pH 4.5 (approximately) is a possible cause of this pain. Vecuronium bromide is reported in contrast to many other neuromuscular blocking agents to cause minimal release of histamine² and indeed no venous sequelae were noted or seen subsequently in the postoperative period even after pain was reported.

We are not aware of other reports of this side-effect, although most injections of vecuronium bromide are in anaesthetised patients and pain will only be noted at the injection site when this anaesthetic technique is used or

when vecuronium bromide is used as pretreatment before suxamethonium.³

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References

1. FOLDES F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs: the priming principle. *British Journal of Anaesthesia* 1984; 56: 663.
2. ROBERTSON EN, BOOU LHDJ, FRAGEN RJ, CRUL JF. Clinical comparison of atracurium and vecuronium (ORG NC 45). *British Journal of Anaesthesia* 1983; 55: 125–9.
3. FERRES CJ, MIRAKHUR RK, CRAIG HJL, BROWNE ES, CLARKE RSJ. Pretreatment with vecuronium as a prophylactic against post-suxamethonium muscle pain. Comparison with other non-depolarizing neuromuscular blocking drugs. *British Journal of Anaesthesia* 1983; 55: 735–41.

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Consent for epidural analgesia

Dr Sneyd's letter (*Anaesthesia* 1987; 42: 1132-3) on this subject saddens me since it reflects a poverty of communication down the years. The matter was thoroughly aired within the Obstetric Anaesthetists' Association (OAA) in the early 1970s. We considered that written consent for an epidural to be administered for labour was no more required than it was for the provision of a pudendal block, a spinal or any other form of pain relief for labour or delivery. Indeed, in my opinion, which I know to be shared by others, for a request to be made for such written consent is contraindicated, since it would bestow a spurious legitimacy upon the contract.

Correspondence from the representatives of the medical defence organisations (conducted when I was President of the OAA) relates to this subject. The advice was that written consent was not required, although it would be 'prudent' to insert in the medical record a note to the effect

that the provision for epidural had been discussed with the mother and that she had agreed to accept the procedure.

My personal opinion is that nowadays, over a decade later, in view of the extensive application of this technique nationally, with an accompanying community familiarity with it, insertion of such a note in the records is prudent only under special circumstances. The latter would include: when epidurals were very infrequently administered in the particular unit; witnesses to the discussion between the mother and the anaesthetist were of doubtful reliability; the mother had previously expressed her strong resistance to the prospect of having an epidural.

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J.S. CRAWFORD

Book reviews

Applied respiratory physiology, 3rd edn	336	Anaesthesia and intensive care for the neurosurgical patient	337
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Applied respiratory physiology

J.F. NUNN. Pp. xvi + 582. Butterworths, 1987. £35.00.

A well-known medical journal uses the question 'What's new in the new editions?' to bring its readers up to date in a few brief lines. Such an approach is quite inappropriate for the third edition of one of anaesthesia's classic texts because, in effect, it is a new book. A little larger and heavier than its predecessors, it benefits enormously from greatly improved production—better contrast, clear lettering, bold headings and good illustrations. This alone is important because the attractive appearance encourages hesitant readers to approach intellectually demanding concepts with greater willingness.

More fundamentally the book has been divided into two parts: basic principles and applications, which occupy about 60 and 40% respectively of the 500 pages. The most remarkable achievement is a breadth of cover far greater than in earlier editions. In part this reflects the concise, clear prose but there is also a very skilful balance between diffuse issues, each condensed into a short but comprehensive and authoritative resumé of principles, and a more discursive approach to subjects at the growing edges, or those which are considered less often in current medical literature. In the clinical sections in particular, there is a pleasing but not too obtrusive personal commentary which reflects the author's opinion of the relative merits of different approaches to treatment, but no hesitation in pointing out where proof is lacking (such as the role of IMV) or cannot be obtained without great difficulty (for instance ARDS).

So where then do faults, if any, lie? It could be argued that the scope is too broad and that much of the information, especially basic principles, is available in smaller, specialised texts. A more restricted content would allow more discussion of detail, more expression of personal opinion and more practical advice. But those who seek more detail are likely to want to follow the current literature (and are given plenty of up-to-date references here), and those who need clinical guidelines should not expect to find them in a textbook of physiology. The generality of readers will be only too grateful to have such a wealth of relevant information condensed between the covers of one, easy-to-handle book. Inevitably there are expressions of opinion to which one can take exception, but that does not detract from the overall merit. Instead it prompts contemplation of the sources of controversy.

It is a mark of our times that the price is exactly five times greater than the first edition (which appeared in 1969), but only foolish anaesthetists would fail to ensure they always have ready access to a copy, preferably their own.

M.A. BRANTHWAITE

Pharmacology and physiology in anesthetic practice

R.K. STOELTING. Pp. xiii + 859. J.B. Lippincott, 1987. \$65.00.

It should be very easy to criticise a work, written by one author, that purports to cover pharmacology and physiology in anaesthetic practice in one volume of less than 1000 pages. Written by Stoelting, though, it is not surprising that serious criticism is unnecessary and inappropriate. The work sets out to encompass physiology and pharmacology strictly relevant to anaesthetic practice, and is written for both students and practitioners of anaesthesia. It is well indexed and clearly and pleasingly illustrated. The logic for separating the index into two parts, a drug index and a subject index is not clear. References are fairly plentiful, but too many refer not to original work but to alternative textbooks of physiology. (There are no fewer than 10 references to Guyton's *Textbook of medical physiology* at the end of the chapter on the physiology of the central nervous system.)

The chapter on the principles of pharmacology has suffered in content, although not in clarity, from the need to be concise. The section on kinetics could usefully be expanded, and receptor theory is considered too briefly. The remainder of the pharmacology section is thorough, well presented and readable. The economy of content is achieved by limiting extensive discussion to the contemporary, and giving commendably little space to those drugs (diethyl ether, trichloroethylene and cyclopropane) which have fallen into disuse over the last decade. An exception to this historical parsimony is the chapter on nonbarbiturate induction agents, which includes substantial sections on alphadione and propanidid, neither of which have been introduced commercially in North America, and both of which have been withdrawn from the European market. Examined controversies in anaesthesia include the old chestnut of halothane hepatitis and the new chestnut of coronary steal due to isoflurane in coronary artery disease. Both are considered in a well balanced and unprejudiced manner.

Although it is not explicit in the title, the physiology covered is almost exclusively the physiology of the normal. No serious attempt is made to consider pathophysiology except in relation to the heart. Pregnancy is apparently also considered a pathological condition since scanty attention is paid to the physiological changes consequent thereon. The nonventilatory role of the lungs similarly receives cursory consideration, and merits only one short paragraph. In all, the physiology section comprises less than one third of the total text and is not so much a reference section as a simple description of fundamental human physiology.

Notwithstanding these reservations this is an excellent

book within the limits the author sets. It will be useful to candidates sitting Part Two of the Fellowship examination and will be an asset to any departmental library. If the American price of \$65 is converted directly into sterling, it will also be good value.

C. GILLBE

Chronic non cancer pain

Edited by S. ANDERSSON, M. BOND, M. MEHTA AND M. SWERDLOW. Pp. 207. MTP Press Ltd, 1987. £12.50.

This book is the product of the International Association for the Study of Pain. It was written to provide a clear text on chronic noncancer pain suitable for physicians with restricted access to the latest techniques of pain relief. The newly launched International Pain Foundation has provided a substantial sum of money to aid distribution of copies of this book in underdeveloped countries. One is left wondering what some will make of it, since there are chapters that require more than basic knowledge for total comprehension, and many of the treatment methods mentioned require resources that may not be available to them.

The authors of the chapters read like a Who's Who of pain relief, although there may be an occasional Who? in more distant parts of the globe than Basingstoke. Overall, the standard of contribution is very high and the basic principles of assessment and treatment of many painful conditions are clearly presented. However, there is redundant material. The reader is given three separate sorts of pain classification not one of which adds much to the treatment of chronic pain. It might have been more worthwhile to curtail some of this and use the extra space for practical matters.

There are examples throughout the book that the view from the ivory tower can become restricted, and it is worthwhile to read each chapter and bear in mind the specialty of the author. It is possible to lose sight of the ideas of other groups of specialists when talking about your own. Readers should look up their chosen topic under every heading in the excellent index, since there may be different opinions expressed elsewhere.

Some contributions are worthy of particular comment. Bond's closing statement in his splendid chapter on the psychology of pain 'that all those dealing with individuals in pain make themselves competent in the examination of the patient's physical and psychological state' should be printed on the front of the notes of all patients who attend a pain clinic. Young's chapter on history, examination and assessment is extremely competent, but too brief; the section on investigation is brief to the point of irrelevancy. There are further solid contributions from Loeser on neurological disease, Jayson on musculoskeletal and rheumatic disease and Cousins, who covers the difficult topic of visceral pain in an easily understood manner.

This reviewer is less happy with the chapters on non-invasive methods, drug control and nerve blocks. The desire to educate developing countries is shown most clearly here, because the range of therapy offered, and the way it is presented, is more superficial than in other parts of the book. In the chapter on drug control of pain, the authors have been restricted to mention only a limited selection of drugs from the World Health Organisation list, and this limits the impact of an otherwise very reasonable chapter, for a wide readership. In addition, there are recommendations with which some may not entirely agree: for example, the chronic use of phenothiazines or benzodiazepines.

One might have hoped for better information about nerve blocks although this view is probably a reflection

of my own prejudices. If one is to instruct inexperienced personnel in the use of therapeutic blockade it is reasonable to set limits to the amounts of drug used and the volume employed, as the authors state. It should also be stated that these maximum doses vary with the site and purpose of injection, otherwise they will serve to inhibit the tiro and infuriate the expert. The descriptions of the blocks are adequate at best and, in the case of stellate ganglion block, could be improved considerably. This reviewer has had several stellate ganglion blocks at C₇ and holds a fervent belief that pneumothorax need not be 'a more common complication' if the block is performed above the cupola of the lung at C₆.

Despite these minor criticisms this book is well written in a clear style, and is well presented. It is not a book for the anaesthetist who practises pain relief, or for the FFA candidate, but given the limitations noted earlier it is reasonable to recommend it as an inexpensive, basic introduction to the diagnosis and treatment of chronic noncancer pain.

J.E. CHARLTON

Anaesthesia and intensive care for the neurosurgical patient

S.M. WILLATTS AND F.J.M. WALTERS. Pp. 337. Blackwell Scientific Publications, 1986. £35.00.

In the foreword to this new textbook the reader is reminded of the importance to the neuroanaesthetist of a background knowledge of the relevant basic sciences, the surgical problems encountered, and a broad knowledge of the range of techniques available. All these are admirably covered in the book. Chapters on neuroanatomy, physiology, and pharmacology contain just the right amount of information, clearly written and well illustrated. An understanding of routine neurosurgical investigations is important to the neuroanaesthetist, since the magnitude and effects of a pathological lesion may be important in the selection of an appropriate anaesthetic technique. This need is met by an excellent chapter on pre-operative neurosurgical investigations and by a concise account of intracranial tumours and their surgical treatment.

Several chapters cover the individual problems of anaesthesia for posterior fossa surgery, vascular lesions, spinal surgery, paediatric neurosurgery, and the very important and progressive aspects of surgery for epilepsy and focal lesions amenable to stereotactic surgery. In each case there is a brief introduction which outlines the clinical aspects, anatomy, and relevant pathology; and succinctly but necessarily didactically presented, the authors' recommendations for their management.

Neurosurgical intensive therapy, which includes the management of head injuries, is an aspect of care in which the anaesthetist, given the opportunity, can make a significant contribution, and the reader will find that all essential aspects of this work are covered.

General profession trainees will find in this book all they need to know about the principles of neurosurgical anaesthesia and intensive care. Anaesthetists practically involved in these aspects in their daily work will find the well-referenced text an informative and up-to-date statement of current practice. The book is excellently produced, and the price, by today's standards, is reasonable.

J.N. HORTON

Anaphylactic reactions in anaesthesia and intensive care

J.H. LEVY. Pp. viii + 173. Butterworths, 1987. £30.00.

In consideration of any new volume, a reviewer has two questions to ask—firstly, is there a need for the book; and

secondly, how does it compare with presently available volumes. There is greater likelihood of the need for anaesthesia on one or more occasions as patients live longer, and so the probable incidence of adverse reactions to anaesthetic drugs will surely increase. Thus, an up-to-date survey of the current literature on adverse reactions in anaesthesia and intensive care would appear important.

The author, an assistant professor of anesthesiology at Emory University School of Medicine, Atlanta, has published previously on the topic of adverse reactions, and is therefore well able to present this lucid, authoritative, if somewhat didactic approach to the subject. The book is divided into two sections, mechanisms and management. The first section offers a good summary of basic immunology of drug reactions for both the examination candidate and for his senior colleague who attempts to grasp current concepts in this rapidly changing subject. Indeed, a review of the references will show that the author has carefully surveyed the literature up to the middle of 1985.

The chapters on the management of adverse anaphylactic and anaphylactoid reactions represent good sound advice. If I had to take exception to any part of the discussion it would be that about skin testing, in elucidation of the mechanism and cause of an adverse reaction. Fisher and his colleagues at the Royal North Shore Hospital, Sydney have advocated this as a valuable tool in diagnosis of the aetiology of adverse reactions (especially those due to muscle relaxants), but other authors are less enthusiastic. Nevertheless, the chapter on 'Pre-operative considerations of the patient at risk' represents an excellent review of current knowledge and practice. It was disappointing that the author did not condemn wholeheartedly the foolhardy practice, still beloved of many anaesthetists, of the 'trying out the effect of a test dose' in a potentially sensitive individual.

There is also little information from the viewpoint of the reader in Europe or Great Britain about the mechanisms and incidence of adverse reactions to Cremophor-solubilised drugs (although Althesin has been withdrawn since this volume was edited; we still use other similarly solubilised

drugs, cyclosporin, vitamin K₁ (Konakion), and miconazole (Daktarin). No mention is made of anaphylactoid reactions to etomidate (Krumholz *et al.*, 1984; Sold and Rothhammer, 1985) or to the emulsion formulation of diazepam (von Dardel *et al.*, 1983; Brogger-Nielsen, 1984). There is also no formal discussion of possible predisposition to adverse reactions (for instance pregnancy, stress) although the concept of cross reactivity between structurally similar compounds is mentioned. The author might also have discussed the question of subclinical reactions to drugs (that is, complement changes which follow drug administration without clinical symptomatology) what is their relevance; how common are they?

These comments are not meant to be critical, rather they represent topics perhaps for inclusion in a second edition; the authors should omit chapter 11, which has little relevance to the rest of the book, and only sketches over current thinking on the aetiology and management of ARDS.

Overall, the author is to be congratulated on a difficult task, well accomplished. The book is reasonably priced, and I can recommend this volume to anyone sitting examinations. It is one for your own bookshelf—rather than relying on the library copy.

J.W. SEAR

Books received

We wish to thank publishers for the titles listed here, some or all of which may be reviewed in future issues of *Anaesthesia*.

Sickle-cell anemia and thalassemia

R.G. HUNTSMAN. Pp. xv + 223. The Canadian Sickle Cell Society, 1987.

Lectures in anaesthesiology 1987/2

Edited by J.S.M. ZORAB. Pp. 108. Blackwell Scientific Publications, 1987.

Anesthesia for thoracic surgery

J.L. BENUMOF. Pp. xii + 521. W.B. Saunders, 1987.

Anaesthetic literature

This section of *Anaesthetic Literature* contains references taken from *Current Contents—Life Sciences* for December 1987. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Abdominal surgery

Dopamine receptors in human gastrointestinal mucosa. HERNANDEZ DE, MASON GA *et al. Life Sciences* 1987; **41**: 2717.

Pharmacology

Adrenergic drugs and their antagonists

Endogenous restoration of noradrenaline by precursor therapy in dopamine-beta-hydroxylase deficiency. BIAGGIONI I, ROBERTSON D. *Lancet* 1987; **2**: 1170.

Effects of beta-adrenergic blockade on the ventilatory responses to hypoxic and hyperoxic exercise in man. CONWAY MA, PETERSEN ES. *Journal of Physiology* 1987; **393**: 43.

Pathways of alpha-a-adrenergic action: comparison with V1-vassopressin and A1-angiotension. GARCIA-SAINZ JA. *Circulation Research* 1987; **61** (Suppl): II-1.

Effect of unnatural noradrenaline precursor on sympathetic control and orthostatic hypotension in dopamine-beta-hydroxylase deficiency. MAN IN 'T VELD AJ, BOOMSMA F *et al. Lancet* 1987; **2**: 1172.

Hypersomnolence with beta-adrenergic blockers. THACHIL J, ZELLER JR, KOCHAR MS. *Chest* 1987; **92**: 943.

Anaesthetic agents

Different effects of halothane on diaphragm and hindlimb muscle in rats. DUREUIL B, VIRES N *et al. Journal of Applied Physiology* 1987; **63**: 1757.

Anaesthesia with alphaxalone plus alphadolone acetate decreases serum concentrations of LH in castrated rats. EMANUELE MA, TENTLER J *et al. Journal of Endocrinology* 1987; **115**: 221.

Relationship between lower oesophageal contractility, clinical signs and halothane concentration during general anaesthesia and surgery in man. EVANS JM, BITHELL JF, VLACHONIKOLIS IG. *British Journal of Anaesthesia* 1987; **59**: 1346.

Nitric oxide (NO) formation from nitrovasodilators occurs independently of hemoglobin or non-heme iron. FEELISCH M, NOACK E. *European Journal of Pharmacology* 1987; **142**: 465.

Central respiratory depression induced by acetylcholinesterase inhibition: involvement of anaesthesia FOUTZ AS, BOUDINOT E, DENAVIT-SAUBIE M. *European Journal of Pharmacology* 1987; **142**: 207.

Intestinal absorption of trichloroethylene in dogs. HOBARA T, KOBAYASHI H *et al. Toxicology and Applied Pharmacology* 1987; **91**: 256.

Cardiovascular status during ketamine anaesthesia in the fetal lamb. LAFOND JS, FOURON J-C, BARD H. *Biology of the Neonate* 1987; **52**: 279.

Threshold hypnotic concentration of methohexitone. LAUVEN PM, SCHWILDEN H, STOECKEL H. *European Journal of Clinical Pharmacology* 1987; **33**: 261.

The effects of halothane on the human beta-adrenergic receptor of lymphocyte membranes. MARTY J, NIVOCHÉ Y *et al. Anesthesiology* 1987; **67**: 974.

Analgesic agents

Influence of pH on the buccal absorption of morphine sulphate and its major metabolite, morphine-3-glucuronide. AL-SAYED-OMAR O, JOHNSTON A, TURNER P. *Journal of Pharmacy and Pharmacology* 1987; **39**: 934.

Sufentanil disposition during cardiopulmonary bypass. FLEZZANI P, ALVIS MJ *et al. Canadian Journal of Anaesthesia* 1987; **34**: 566.

Methods used for the study of opioid receptors. LESLIE FM. *Pharmacological Reviews* 1987; **39**: 197.

The pharmacokinetics of intravenous, intramuscular, and subcutaneous nalbuphine in healthy subjects. LO MW, LEE FH *et al. European Journal of Clinical Pharmacology* 1987; **33**: 297.

Investigation of the antinociceptive activity of buprenorphine in sheep. NOLAN A, LIVINGSTON A, WATERMAN AE. *British Journal of Pharmacology* 1987; **92**: 527.

Morphine-6-glucuronide, a potent Mu agonist. PASTERNAK GW, BODNAR RJ *et al. Life Sciences* 1987; **41**: 2845.

A dose-response study with nalbuphine hydrochloride for pain in patients after upper abdominal surgery. PUGH GC, DRUMMOND GB. *British Journal of Anaesthesia* 1987; **59**: 1356.

Constant I.V. infusions of nalbuphine or buprenorphine for pain after abdominal surgery. PUGH GC, DRUMMOND GB *et al. British Journal of Anaesthesia* 1987; **59**: 1364.

Morphine sulfate depression of cardiac function is attenuated by opiate receptor antagonism with naloxone. VARGISH T, BEAMER KC *et al. Circulatory Shock* 1987; **23**: 189.

Minireview: Immunomodulation by morphine and marijuana. YAHYA MD, WATSON RR. *Life Sciences* 1987; **41**: 2503.

Nalbuphine as an analgesic component in balanced anaesthesia for cardiac surgery. ZSIGMOND EK, WINNIE AP *et al. Anesthesia and Analgesia* 1987; **66**: 1155.

Muscle relaxants

Metocurine kinetics in patients undergoing operations requiring cardiopulmonary bypass. AVRAM MJ, SHANKS CA *et al. Clinical Pharmacology and Therapeutics* 1987; **42**: 576.

The effect of procainamide on plasma cholinesterase activity. KAMBAM JR, NAUKAM RJ, SASTRY BVR. *Canadian Journal of Anaesthesia* 1987; **34**: 579.

Dantrolene prevents the malignant hyperthermic syndrome by reducing free intracellular calcium concentration in skeletal muscle of susceptible swine. LOPEZ JR, ALLEN P *et al. Cell Calcium* 1987; **8**: 385.

Anticholinergic drugs. WEINER MF, DAVIS KL In: BURROWS *et al. eds. Antimanics, anticonvulsants and other drugs in psychiatry*. Amsterdam: Elsevier Sci, 1987; 191.

Other drugs

Bone marrow hypoplasia during intensive care: bone marrow culture studies implicating ranitidine in the suppression of haemopoiesis. AMOS RJ, KIRK B *et al. Human Toxicology* 1987; **6**: 503.

- Antidepressant drugs and down-regulation of presynaptic receptors. FINBERG JPM. *Biochemical Pharmacology* 1987; **36**: 3557.
- Ranitidine disposition in severe hepatic cirrhosis. GONZALEZ-MARTIN G, PAULOS C *et al.* *International Journal of Clinical Pharmacology—Therapy and Toxicology* 1987; **25**: 139.
- Recombinant tissue plasminogen activator: a brief review. GROSS-BARD EB. *Pharmaceutical Research* 1987; **4**: 375.
- Cyclic GMP synthesis and function. WALDMAN SA, MURAD F. *Pharmacological Reviews* 1987; **39**: 163.

Apparatus

- Central venous dialysis access—experience with a dual-lumen, silicone rubber catheter. DUNN J, NYLANDER W, RICHIE R. *Surgery* 1987; **102**: 784.
- Variations in the flow of cerebrospinal fluid through spinal needles. GERRISH SP, PEACOCK JE. *British Journal of Anaesthesia* 1987; **59**: 1465.

Complications

- Intrathoracic complications of acute pancreatitis. BASRAN GS, RAMASUBRAMANIAN R, VERMA R. *British Journal of Diseases of the Chest* 1987; **81**: 326.
- Precipitous bradycardia induced by laryngoscopy in cardiac surgical patients. PODOLAKIN W, WELLS DG. *Canadian Journal of Anaesthesia* 1987; **34**: 618.
- Contact 400: a possible cause of aspiration under anaesthesia. WILKINSON DJ. *Human Toxicology* 1987; **6**: 529.

General anaesthetic procedures

- Use of sodium nitroprusside induced hypotensive anaesthesia for reducing blood loss in patients undergoing lienorenal shunts for portal hypertension. SOOD S, JAYALAXMI TS *et al.* *British Journal of Surgery* 1987; **74**: 1036.
- Anticoagulants in anaesthesia. STOW PJ, BURROWS FA. *Canadian Journal of Anaesthesia* 1987; **34**: 632.

General interest

- Controllable and uncontrollable stress in humans—alterations in mood and neuroendocrine and psychophysiological function. BREIER A, ALBUS M *et al.* *American Journal of Psychiatry* 1987; **144**: 1419.
- Hypokalemia complicating Duchene muscular dystrophy. McDONALD B, ROSENTHAL SA. *The Yale Journal of Biology and Medicine* 1987; **60**: 405.
- Non-A, Non-B hepatitis. THOMAS HC. *Quarterly Journal of Medicine* 1987; **65**: 793.

Local analgesia

- Transurethral incision of the prostate under local anaesthesia in high-risk patients: a pilot study. GRAVERSEN PH, GASSER TC *et al.* *Scandinavian Journal of Urology and Nephrology* 1987; **104** (Suppl. 21): 87.
- Comparison on pain associated with intradermal and subcutaneous infiltration with various local anesthetic solutions. MORRIS R, MCKAY W, MUSHLIN P. *Anesthesia and Analgesia* 1987; **66**: 1180.
- Inhibition of human serum and rabbit muscle cholinesterase by local anesthetics. PEREZ-GUILLERMO F, DELGADO EM, VIDAL CJ. *Biochemical Pharmacology* 1987; **36**: 3593.

Spinal and epidural analgesia

- Spinal anesthesia with hyperbaric lidocaine and bupivacaine: effects of epinephrine on the plasma concentration profiles. BURM AGL, VAN KLEEF JW *et al.* *Anesthesia and Analgesia* 1987; **66**: 1104.

Spinal opioids

- Comparative pharmacokinetics of spinal opioids in humans: a step toward determination of relative safety. COUSINS MJ. *Anesthesiology* 1987; **67**: 875.
- Effects of temperature on the interaction of morphine with opioid

receptors. PUIG MM, WARNER W *et al.* *British Journal of Anaesthesia* 1987; **59**: 1459.

Pharmacokinetics of epidural morphine and morphine and meperidine in humans. SJOSTROM S, HARTVIG P *et al.* *Anesthesiology* 1987; **67**: 877.

Pharmacokinetics of intrathecal morphine and meperidine in humans. SJOSTROM S, TAMSEN A *et al.* *Anesthesiology* 1987; **67**: 889.

Obstetric anaesthesia and analgesia

The epidural test dose in obstetrics. Is it necessary? DAIN SL, ROLBIN SH, HEW EM. *Canadian Journal of Anaesthesia* 1987; **34**: 601.

Evaluation of 1-deamino-[D-Tyr (Oethyl) 2, Thr4, Orn8]vasotocin, an oxytocin antagonist, in animal models of uterine contractility and preterm labor HAHN DW, DEMAREST KT *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157** Part 1: 977.

Fentanyl droperidol supplementation of rapid sequence induction in the presence of severe pregnancy-induced and pregnancy-aggravated hypertension. LAWES EG, DOWNING JW *et al.* *British Journal of Anaesthesia* 1987; **59**: 1381.

Low-dose aspirin in prevention of toxemia of pregnancy: does it have a place? LUBBE WF. *Drugs* 1987; **34**: 515.

Cardiac output during labour. ROBSON SC, DUNLOP W *et al.* *British Medical Journal* 1987; **295**: 1169.

Paediatric anaesthesia and intensive care

Pain and its effects in the human neonate and fetus. ANAND KJS, HICKEY PR. *New England Journal of Medicine* 1987; **317**: 1321.

Growth hormone-releasing hormone. Studies in cord blood from term human newborns. ARGENTE J, ACQUAFREDDA A *et al.* *Biology of the Neonate* 1987; **52**: 264.

Oxygen—use and monitoring. BRADBURN NC. In: SCHREINER RL, BRADBURN NC eds. *Care of the newborn*, 2nd edn. New York: Raven Press, 1988: 99.

Fluid and electrolyte management. BRADBURN NC, LEMONS JA. In: SCHREINER RL, BRADBURN NC, eds. *Care of the newborn*, 2nd edn. New York: Raven Press, 1988: 146.

Apnea. BRADBURN NC, SCHREINER RL. In: SCHREINER RL, BRADBURN NC eds. *Care of the newborn*, 2nd edn. New York: Raven Press, 1988: 113.

Nifedipine: Effects on fetal and maternal hemodynamics in pregnant sheep. HARAKE B, GILBERT RD *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157** Part 1: 1003.

Indicators of perinatal asphyxia. HOLLANDER DI, WRIGHT L *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157** Part 1: 839.

Surfactant for the treatment of respiratory distress syndrome. JOBE A, IKEGAMI M. *American Review of Respiratory Disease* 1987; **136**: 1256.

Umbilical cord blood pH and Apgar scores as an index of neonatal health. JOSTEN BE, JOHNSON TRB, NELSON JP. *American Journal of Obstetrics and Gynecology* 1987; **157** Part 1: 843.

Developmental changes in the ventilatory response of the newborn to added airway resistance. LAFRAMBOISE WA, STANDAERT TA *et al.* *American Review of Respiratory Disease* 1987; **136**: 1075.

Temperature regulation. LEMONS JA, BRADBURN NC. In: SCHREINER RL, BRADBURN NC eds. *Care of the newborn*, 2nd edn. New York: Raven Press, 1988: 42.

An assessment of children's pain: a review of behavioral, physiological and direct scaling techniques. McGRATH PA. *Pain* 1987; **31**: 147.

The use of fetal neuromuscular blockade during intrauterine procedures. MOISE KJ JR, CARPENTER RJ JR *et al.* *American Journal of Obstetrics and Gynecology* 1987; **157** Part 1: 874.

Common carotid artery flow velocity measurements in the newborn period with pulsed Doppler technique. RAJU TNK, GO M *et al.* *Biology of the Neonate* 1987; **52**: 241.

Nasal respiratory resistance in cleft lip and palate. SANDHAM A, SOLOW B. *Journal of Cleft Palate* 1987; **24**: 278.

Resuscitation. SCHREINER RL, BRADBURN NC, KEENER PA. In: SCHREINER RL, BRADBURN NC eds. *Care of the newborn*, 2nd edn. New York: Raven Press, 1988: 6.

The effects of general anesthesia on upper respiratory tract infections in children. TAIT AR, KNIGHT PR. *Anesthesiology* 1987; **67**: 930.

- Working of breathing. ZAPLETAL A, SAMANEK M, PAUL T. In: ZAPLETAL A *et al.* *Lung function in children and adolescents*. Basel: S. Karger, 1987: 68.
- Lung elasticity. ZAPLETAL A, SAMANEK M, PAUL T. In: ZAPLETAL A *et al.* *Lung function in children and adolescents*. Basel: S. Karger, 1987: 13.
- Static lung volumes and lung ventilation. ZAPLETAL A, SAMANEK M, PAUL T. In: ZAPLETAL A *et al.* *Lung function in children and adolescents*. Basel: S. Karger 1987: 4.
- Alveolar ventilation, respiratory functional dead space and its ventilation, oxygen consumption and elimination of carbon dioxide. ZAPLETAL A, SAMANEK M, PAUL T. In: ZAPLETAL A *et al.* *Lung function in children and adolescents*. Basel: S. Karger, 1987: 83.

Cardiovascular system

Physiology

- Importance of venous return, venous resistance, and mean circulatory pressure in the physiology and management of shock. BRESSACK MA, RAFFIN TA. *Chest* 1987; **92**: 906.
- Model analysis of the enhancement of tissue oxygenation by hemodilution due to increased microvascular flow velocity. MIRHASHEMI S, ERTEFAJ S *et al.* *Microvascular Research* 1987; **34**: 290.
- Cardiac transplantation. SCHROEDER JS, HUNT S. *Journal of the American Medical Association* 1987; **258**: 3142.
- Atrial natriuretic peptide levels and coronary heart disease. SILKE B. *International Journal of Cardiology* 1987; **17**: 277.
- Endotoxemia in burn patients—levels of circulating endotoxins are related to burn size. WINCHURCH RA, THUPARI JN, MUNSTER AM. *Surgery* 1987; **102**: 808.
- Autonomic control of large coronary arteries and resistance vessels. YOUNG MA, KNIGHT DR, VATNER SF. *Progress in Cardiovascular Diseases* 1987; **30**: 211.

Treatment and medication

- Elevated pulmonary vascular resistance and cardiac transplantation. ADDONIZIO LJ, GERSONY WM *et al.* *Circulation* 1987; **76** (Suppl.): 52.
- Surgical outcome in chronic aortic regurgitation—a physiologic framework for assessing preoperative predictors. BOROW KM. *Journal of the American College of Cardiology* 1987; **10**: 1165.
- Interactions of amiodarone with digoxin in rats. BRAUNSCHWEIG J, STAUBLI M, STUDER H. *British Journal of Pharmacology* 1987; **92**: 553.
- Encainide: a review of its pharmacological properties and therapeutic efficacy. BROGDEN RN, TODD PA. *Drugs* 1987; **34**: 519.
- Clinical assessment of extracellular fluid volume in hyponatremia. CHUNG H, KLUGE R *et al.* *American Journal of Medicine* 1987; **83**: 905.
- The automatic implantable cardioverter-defibrillator in drug-refractory tachyarrhythmias. FOGOROS RN, FIEDLER SB, ELSON JJ. *Annals of Internal Medicine* 1987; **107**: 635.
- Emergency coronary bypass for cardiogenic shock. GUYTON RA, ARCIDI JM *et al.* *Circulation* 1987; **76** (Suppl): 22.
- Pancreatic response to crystalloid resuscitation in experimental pancreatitis. KNOL JA, INMAN MG *et al.* *Journal of Surgical Research* 1987; **43**: 387.
- New antiarrhythmic drugs: tocainide, mexiletine, flecainide, encainide, and amiodarone. KREEGER RW, HAMMILL SC. *Mayo Clinic Proceedings* 1987; **62**: 1033.
- The pharmacokinetics of lignocaine and beta-adrenoceptor antagonists in patients with acute myocardial infarction. NATTEL S, GAGNE G, PINEAU M. *Clinical Pharmacokinetics* 1987; **13**: 293.
- Continuous monitoring of mixed venous oxygen saturation during aortic surgery. SHENAO SA, CASAR G *et al.* *Chest* 1987; **92**: 796.
- Interactions of dihydralazine with furosemide in hypertonic patients. SIEGMUND W, KAIRIES M *et al.* *International Journal of Clinical Pharmacology—Therapy and Toxicology* 1987; **25**: 148.
- Pre-treatment with beta-blockers and the frequency of hypokalaemia in patients with acute chest pain. SIMPSON E, RODGER JC *et al.* *British Heart Journal* 1987; **58**: 499.
- Reduction of perioperative hemorrhage by anterior mediastinal spray. Application of fibrin glue during cardiac operations.

- SPOTNITZ WD, DALTON MS *et al.* *Annals of Thoracic Surgery* 1987; **44**: 529.
- Cardiovascular effects of verapamil in essential hypertension. STADLER P, LEONARDI L *et al.* *Clinical Pharmacology and Therapeutics* 1987; **42**: 485.
- Bubble oxygenation and cardiomyotomy suction impair the host defense during cardiopulmonary bypass: a study in dogs. VAN OEVEREN W, DANKERT J, WILDEVUUR CRH. *Annals of Thoracic Surgery* 1987; **44**: 523.
- Adenosine causes transient dilation of coronary arteries in man. WATT AH, PENNY WJ *et al.* *British Journal of Clinical Pharmacology* 1987; **24**: 665.

Respiration

Physiology

- Mixed venous blood oxygen tension is not a good predictor of survival in patients with chronic obstructive lung disease. CHODOSOWSKA E, SKWARSKI K, ZIELINSKI J. *European Journal of Respiratory Diseases* 1987; **71**: 233.
- Ventilation during sleep onset. COLRAIN IM, TRINDER J *et al.* *Journal of Applied Physiology* 1987; **63**: 2067.
- Hyperventilation and panic disorder. COWLEY DS, ROY-BRYNE PP. *American Journal of Medicine* 1987; **83**: 929.
- Effects of phrenic nerve cooling on diaphragmatic function. DUREUIL B, VIRES N *et al.* *Journal of Applied Physiology* 1987; **63**: 1763.
- Sternomastoid muscle function and fatigue in breathless patients with severe respiratory disease. EFTHIMIOU J, FLEMING J, SPIRO SG. *American Review of Respiratory Disease* 1987; **136**: 1099.
- The close but mysterious ties between obstructive sleep apnea and the obesity-hypoventilation syndrome. FINDLEY LJ. *Chest* 1987; **92**: 772.
- Temperature affects lung fluid and recoil during high tidal ventilation at low resting volume. HORIE T, IZUMI T *et al.* *Journal of Applied Physiology* 1987; **63**: 1705.
- Interaction of hypercapnia and phasic volume feedback on motor control of the upper airway. KUNA ST. *Journal of Applied Physiology* 1987; **63**: 1744.
- Angiotensin-converting enzyme and the cough reflex. MORICE AH, LOWRY R *et al.* *Lancet* 1987; **2**: 1116.
- Relationship of respiratory drives to dyspnea and exercise performance in chronic obstructive pulmonary disease. ROBINSON RW, WHITE DP, ZWILLICH CW. *American Review of Respiratory Disease* 1987; **136**: 1084.
- Concerning the importance of pharyngeal muscles in the maintenance of upper airway patency during sleep—an opinion. STROHL KP, OLSON LG. *Chest* 1987; **92**: 918.
- Grading of dyspnoea and walking speed in cardiac disease and in chronic airflow obstruction. WARLEY ARH, FINNEGAN OC *et al.* *British Journal of Diseases of the Chest* 1987; **81**: 349.
- Regional extravascular density of the lung in patients with acute pulmonary edema. WOLLMER P, RHODES CG *et al.* *Journal of Applied Physiology* 1987; **63**: 1890.
- Comparison of arterial-end-tidal PCO_2 difference and dead space/tidal volume ratio in respiratory failure. YAMANAKA MK, SUE DY. *Chest* 1987; **93**: 832.

Treatment and medication

- Ventilatory muscle dysfunction in patients with idiopathic diaphragmatic paralysis, reversal by intermittent external negative pressure ventilation. CELLI BR, RASSULO J, CORRAL R. *American Review of Respiratory Disease* 1987; **136**: 1276.
- Nebulised adrenaline in acute severe asthma: comparison with salbutamol. COUPE MO, GULY U *et al.* *European Journal of Respiratory Diseases* 1987; **71**: 227.
- Nosocomial pneumonia in intubated patients given sucralate as compared with antacids or histamine type 2 blockers: the role of gastric colonization. DRIKS MR, CRAVEN DE *et al.* *New England Journal of Medicine* 1987; **317**: 1376.
- Effects of aminophylline on respiratory drive and neuromuscular coupling in normal man and in patients with chronic airflow obstruction. GIGLIOTTI F, SPINELLI A *et al.* *European Journal of Clinical Pharmacology* 1987; **33**: 231.
- Effects of an anticholinergic bronchodilator on arterial blood gases of hypoxemic patients with COPD—comparison with a beta-

- adrenergic agent. GRASS NJ, BANKWALA Z. *American Review of Respiratory Disease* 1987; **136**: 1091.
- Hypokalaemia and other non-bronchial effects of inhaled fenoterol and salbutamol: a placebo-controlled dose-response study in healthy volunteers. SCHEININ M, KOULU M *et al. British Journal of Clinical Pharmacology* 1987; **24**: 645.
- Preoperative assessment of pulmonary function. WOLFE WG. *Annals of Thoracic Surgery* 1987; **44**: 562.

Central nervous system

Physiology

- Reminiscences on the sodium pump. DEAN RB. *Trend in Neuro-Sciences* 1987; **10**: 451.
- Cerebral circulation: effects of sympathetic nerves and protective mechanisms during hypertension. FARACI FM, MAYHAN WG *et al. Circulation Research* 1987; **61**: II-102.
- Stress-induced insomnia: opioid-dopamine interactions. FRATTA W, COLLU M *et al. European Journal of Pharmacology* 1987; **142**: 437.
- Experimental intracerebral mass—time-related effects on local cerebral blood flow. KINGMAN TA, MENDELOW AD *et al. Journal of Neurosurgery* 1987; **67**: 732.
- Integrative physiological studies of peptides in the central nervous system. NAYLOR AM, RUWE WD, VEALE WL. In: BOULTON AA, BAKER GB, PITTMAN QJ. *Peptides*. Clifton: Humana Press Inc., 1987: 349.
- Neuropsychological disturbances in hemiparkinsons disease. STARKSTEIN S, LEIGUARDA R *et al. Neurology* 1987; **37**: 1762.
- The acute cerebral effects of changes in plasma osmolality and oncotic pressure. ZORNOW MH, TODD MM, MOORE SS. *Anesthesiology* 1987; **67**: 936.

Treatment and medication

- Role of dopamine in ischemic striatal injury—metabolic evidence. GLOBUS MYT, GINSBERG MD *et al. Neurology* 1987; **37**: 1712.
- Mode of action of anticonvulsant drugs. EADIE MJ. In: BURROWS *et al. eds. Antimanics, anticonvulsants and other drugs in psychiatry*. Amsterdam: Elsevier Sci. 1987; 113.
- The effects of antidepressants on the cerebrospinal fluid homovanillic acid/5-hydroxyindoleacetic acid ratio. RISBY ED, HSIAO JK *et al. Clinical Pharmacology and Therapeutics* 1987; **42**: 547.
- Protection against spinal cord ischemia with insulin-induced hypoglycemia. ROBERTSON CS, GROSSMAN RG. *Journal of Neurosurgery* 1987; **67**: 739.

Endocrine and metabolic

Physiology

- Effects of extracellular fluid volume changes on renal response to low-dose dopamine infusion in normal women. AGNOLI GC, CACCIARI M *et al. Clinical Physiology* 1987; **7**: 465.
- Diabetic polyneuropathy and insulin secretion in type II diabetic patients. AIELLO I, ROSATI G *et al. European Neurology* 1987; **27**: 251.

- Plasma amino acid clearance as an indicator of hepatic function and high-energy phosphate in hepatic ischaemia. BECKER W, KONSTANTINIDES F *et al. Surgery* 1987; **102**: 777.
- Adult respiratory distress syndrome in an adolescent with diabetic ketoacidosis. BREIDBATT S, SINGER L *et al. Journal of Pediatrics* 1987; **111**: 736.
- Insulin resistance in patients with colorectal cancer. COPELAND GP, LEINSTER SJ *et al. British Journal of Surgery* 1987; **74**: 1031.
- Adrenergic system & carbohydrate metabolism—effects of beta blockade on insulin secretion & peripheral insulin sensitivity in normoglycaemic patients. FERRARA LA, CAPALDO B *et al. European Journal of Clinical Pharmacology* 1987; **33**: 273.
- Dual effect of beta-endorphin on insulin secretion in man. GIUGLIANO D, COZZOLINO D *et al. Hormone and Metabolic Research* 1987; **19**: 502.
- Changes in the plasma sodium concentration minor, moderate and major surgery. GUY AJ, MICHAELS JA, FLEAR CTG. *British Journal of Surgery* 1987; **74**: 1027.
- The effects of cortisol supplementation on the metabolic and hormonal response to surgery. LACOURMONTA S, YEO TH *et al. Clinical Physiology* 1987; **7**: 455.
- Neuroendocrinology of pituitary hormone regulation. LECHAN RM. *Endocrinology and Metabolism Clinics of North America* 1987; **16**: 475.
- The role of neuroendocrine abnormalities in the enhanced sodium and water retention of chronic heart failure. McMURRAY J, STRUTHERS AD. *Pharmacology and Toxicology* 1987; **61**: 209.
- Impaired neutrophil function during anesthesia and surgery is due to serum factors. MEALY K, O'FARRELLY C *et al. Journal of Surgical Research* 1987; **43**: 393.
- Effect of insulin-induced hypoglycemia on circulating levels of plasma growth hormone-releasing hormone and somatostatin in children. ROSSKAMP R, BECKER M *et al. Hormone Research* 1987; **27**: 121.
- Dopaminergic regulation of extrarenal potassium metabolism. SAGER PT, DEFONZO RA. *Mineral and Electrolyte Metabolism* 1987; **13**: 385.
- Clinical and hemodynamic correlates of elevated plasma arginine vasopressin after acute myocardial infarction. SCHALLER MD, NUSSBERGER J *et al. American Journal of Cardiology* 1987; **60**: 1178.
- Effect of naloxone on oxytocin and vasopressin release during vaginocervical stimulation in the goat. SECKL JR, LIGHTMAN SL. *Journal of Endocrinology* 1987; **115**: 317.
- Endogenous vasopressin affects postural control of blood pressure in man. SIMPSON HCR, ZUBILLAGA JE *et al. Clinical Sciences* 1987; **73**: 589.

Treatment and medication

- Renin inhibitors. GREENLEE WJ. *Pharmaceutical Research* 1987; **4**: 364.
- Severe symptomatic hyponatremia: treatment and outcome: a study of 64 cases. STERN RH. *Annals of Internal Medicine* 1987; **107**: 656.
- Carbicarb—an effective substitute for NAHCO₃ for the treatment of acidosis. SUN JH, FILLEY GF *et al. Surgery* 1987; **102**: 835.
- Management of attacks of acute porphyria. YEUNG LAJWAH AH, MCCOLL KEL. *Drugs* 1987; **34**: 604.

Obituaries

- Bereen**, James Frederick, OBE, MB, BCH, BAO, FFARCS, FFARCSI, formerly Consultant Neuroanaesthetist at the Royal Victoria Hospital. Qualified from Queen's University, Belfast in 1937.
- Burkinshaw**, Eric, MB, MChir, formerly Consultant Anaesthetist in Sheffield. Qualified from Cambridge in 1954.
- Cousineau**, G, MD, late of Montreal, Canada.
- Evans**, Andrew Richard, MA, BA, MRCS, LRCP, FFARCS, formerly Consultant Anaesthetist at Poole General Hospital. Qualified from Cambridge University in 1960.
- Flowerdew**, Frank Digby Mackworth, MRCS, LRCP. Qualified from St Thomas's Hospital in 1937.
- Goodhart**, Charles Edward Douglas Heron, MA, MD, MB, BChir, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist at St Helier Hospital, Carshalton. Qualified from Cambridge University in 1931.
- Jones**, Olive Marjorie Gordon, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist to United Oxford Hospitals. Qualified from London University in 1928.
- Middleton-Price**, John, MB, MRCS, LRCP, FFARCS, DA, formerly Senior Consultant Anaesthetist at Bethnel Green Hospital. Qualified from London University in 1949.
- Thompson**, Adam Venmore, MB, BS, FFARCS, formerly Registrar at St Mary's Hospital. Qualified from St Mary's Hospital Medical School in 1981.
- Thornton**, Harry Lestock, MRCS, LRCP, FFARCS, DA, formerly Honorary Consulting Anaesthetist to St Mary's Hospital, London. Qualified from St Mary's Hospital London in 1937.
- Watson**, Kathleen Mary, MB, MS, MRCS, LRCP, FFARCS, DA, formerly Consultant Anaesthetist with the Oldham Group of Hospitals. Qualified from London University in 1942.
- Young**, John Victor Innes, MB, BS, FFARCS, DA, formerly Junior Specialist Anaesthetics RAMC. Qualified from London University in 1951.

International congress calendar

1988

- 5-8 April**. Nottingham. *Junior Anaesthetists' Group Annual Meeting*.
Information: Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.
- 15-17 April**. Washington, DC. *Fourth Annual Cherry Blossom Anaesthesia Conference: Patient Safety and Monitoring*.
Information: Georgetown University Medical Centre, Office of Continuing Medical Education, 3800 Reservoir Road, N.W. Washington, DC 20007.
- 23-27 April**. Miami, Florida. *Miami Comprehensive Review Course in Anesthesiology*.
Information: Professional seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.
- 25-27 April**. Intercontinental Hotel, Vienna, Austria. *1st International Symposium on Echocardiography and Doppler in Cardiac Surgery*.
Information: Werner Mohl, MD, c/o Cosmos, The Travel Agency, Kartner Ring 15, A-1015 Vienna, Austria.
- 1-6 May**. Brisbane. *Annual Scientific Meeting of the Faculty of Anaesthetists and Royal Australian College of Surgeons*.
Information: Administrative Officer, Faculty of Anaesthetists, RACS Spring Street, Melbourne 3000, Australia.
- 11-13 May**. Sydney, Australia. *5th International Dental Congress on Modern Pain Control*.
Information: Australian Convention and Travel Services (ACTS), P.O. Box 1929, Canberra, ACT 2601, Australia.
- 16-19 May**. Cancun, Mexico. *1st International Symposium of Quantitative Anaesthesia*.
Information: Dr R. Samayoa de Leon, 18 av. 'B' 0-03, zona 15 Ciudad Guatemala, Guatemala, CA.
- 16-20 May**. US Grant Hotel, San Diego, California. *Fifth International Symposium: Computing in Anaesthesia and Intensive Care*.
Information: UC San Diego School of Medicine, Office of Continuing Medical Education, M-017 La Jolla, California 92093 (619) 534-3940, USA.
- 22-28 May**. Washington, DC. *9th World Congress of Anaesthesiology*.
Information: American Society of Anaesthesiologists, 515 Busse Highway, Park Ridge, Illinois 60068, USA.
- 3-4 June**. La Villette International Conference Center, Paris. *MARPAP 1988*.
Information: Secretariat, MAPAR, Departement d'Anesthesiologie, Hopital de Bicetre, 78 rue du General Leclerc, F-94275, Le Kremlin-Bicetre Cedex, France.
- 5-8 June**. Fontana, Wisconsin. *Eleventh Annual Conference on Shock*.
Information: The Shock Society, Dr Sherwood M. Reichard, Medical College of Georgia, Augusta, GA 30912, USA.
- 8-10 June**. Lyon-Villeurbanne—France. *European Association of Cardiothoracic Anaesthesiologists, 3rd Meeting*.
Information: PG Promotion, 17 Rue Childebert, 69002 Lyon, France.
- 11-16 June**. Cannes, France. *American and European Views on Critical Care*.
Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.
- 14-18 June**. Baveno-Stresa, Lago Maggiore. *4th European Congress on Intensive Care Medicine*.
Information: Organizing Secretariat, MGR, Piazza S. Ambrogio, 16, 20123 Milan, Italy.
- 25-29 June**. Halifax, Nova Scotia. *Canadian Anaesthetists' Society Annual Meeting*.
Information: Dr G. Houle, 187 Gerrard Street E, Toronto, Ontario, Canada, M5A 2E5.
- 7-10 September**. Rome. *10th Annual Meeting of the European Academy of Anaesthesiology*.
Information: EAA Secretariat, Istituto Anestesiologia, Univ. Cattolica S. Cuore, Largo A Gemelli 8, 00186 Rome, Italy.
- 10-14 September**. Florence. *3rd International Symposium*.
Information: Professor M. Zoppi, Cespi Fondazione Pro Juventute, Via Imprunetana 124, 500200 Monteriolo, Florence, Italy.

14-16 September. Cambridge. *Royal College of Surgeons Annual Meeting.*

Information: The Royal College of Surgeons, Lincolns Inn Fields, London WC2.

14-16 September. Southampton. *Linkman Conference and Annual Scientific Meeting & Exhibition.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

14-17 September. Brussels. *5th International Congress Belgian Society of Anesthesia.*

Information: Professor F. Camu, AZ.VU, Laarbeeklaan 101, B-1090 Brussels, Belgium.

1 October. Pavia. *National Congress Societa Italiana di Anest, Rianimazione e Terapia Intensiva.*

Information: Dr G. Conti, SIARRTI, Universita degli Studi, La Sapienza di Roma, Viale del Policlinico, 00161 Roma, Italy.

8-12 October. San Francisco. *Annual Meeting of the American Society of Anesthesiologists.*

Information: John W. Andes, Executive Secretary, 515 Busse Highway, Park Ridge III 60068, USA.

13-15 October. Mainz, Federal Republic of Germany. *7th Annual Meeting of the European Society of Regional Anaesthesia.*

Information: Klinikum fur Anesthesiologie, Postfach 3960, Langenbeckstrasse 1, 6500 Mainz, Federal Republic of Germany.

23-28 October. Rio de Janeiro. *World Congress of Gynecology and Obstetrics.*

Information: Professor Paulo Belfort, Av. Armando Lombardi, 800/223 Barra da Tijuca, 22600 Rio de Janeiro RJ, Brazil.

29 October-2 November. Ballarat, Victoria. *Annual General Meeting Australian Society of Anaesthetists.*

Information: The Secretariat, ASA, PO Box 600, Edgecliff, New South Wales 2027, Australia.

6-11 November. Penediente, Brazil. *XXXV Brazilian Congress of Anaesthesiology.*

Information: Soc. Brazilene Anest., Rua Prof. Alfredo Gomez 36 CEP-22251, Rio de Janeiro, Brazil RJ.

9-12 November. Tauranga, New Zealand. *Conference of Anaesthetists of New Zealand.*

Information: Dr M. Hugel, Conference Secretary, Department of Anaesthetics, Tauranga Hospital, Private Bag, Tauranga, New Zealand.

17-24 December. Colorado. *Current Issues in Medicine.*

Information: Professional Seminars/University of Miami, P.O. Box 012318, Miami, Florida 33101, USA.

1989

11-14 May. Rotterdam. *Second European Congress of Paediatric Anaesthesia.*

Information: Mrs J.F. Aukes-Jager, Sophia Children's Hospital, Department of Paediatric Anaesthesia, Gordelweg 160, NL-3038 GE Rotterdam.

9-13 June. Ottawa. *Joint Meeting with the Canadian Anaesthetists' Society.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

26-30 June. Copenhagen. *20th Scandinavian Congress.*

Information: Professor S.H. Johansen, Herlev Hospital, DK 2730 Herlev, Denmark.

12-16 August. Christchurch, New Zealand. *Combined Meeting New Zealand Society of Anaesthetists and Australian Society of Anaesthetists.*

Information: ASA, Box 600, Edgecliff, NSW 2027, Australia.

1-4 September. Tunisia. *3rd Pan Arab Congress on Anaesthesia and Intensive Care.*

Information: Dr Jamal Al-Shanableh, P.O. Box 15404, Marka-Amman, Jordan.

3-8 September. Kyoto, Japan. *Fifth World Congress on Intensive and Critical Care Medicine.*

Information: The Fifth World Congress on Intensive and Critical Care Medicine, c/o Japan Convention Services Inc., Nippon Press Center Building, 2-2-1 Uchisaiwai-cho, Chiyoda-ku, Tokyo 100, Japan.

12-16 September. Austria. *International Conference on Anaesthesia, Intensive Care and Emergency Medicine.*

Information: Professor Doctor J.M. Hackl, University Klinik fur Anaesthesie und Allg. Intensivmedizin, Anichstr. 35, A-6020 Innsbruck, Austria.

13-15 September. Swansea. *Linkman Conference and Annual Scientific Meeting and Exhibition.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

14-15 September. Osaka, Japan. *4th International Symposium of Endocrinology in Anaesthesia and Surgery.*

Information: Department of Anesthesiology, University of Hiro-saki, School of Medicine, 5 Zaifu-cho, Hiro-saki, Aomori-ken, 036 Japan.

1990

9-15 September. Warsaw. *VIIIth European Congress of Anaesthesiology.*

Information: The Organising Committee, VIIIth European Congress of Anaesthesiology, c/o Polish Society of Anaesthesiology & Intensive Therapy, ul. Kasprzaka 17a, 01-211 Warsaw, Poland.

26-28 September. Manchester. *Linkman Conference and Annual Scientific Meeting and Exhibition.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

1992

29 March-2 April. Atlanta, Georgia. *The Third International Symposium on the History of Anaesthesia.*

Information: R.K. Calverley, MD, Clinical Professor of Anesthesiology, Medical Center, University of California, 225 Dickinson Street, San Diego, California CA 92103-1990, USA.

14-19 June. The Hague. *10th World Congress of Anaesthesiology.*

Information: Dr Harm Lip, Nilantweg 99, 8041 AR Zwolle, Netherlands.

1993

September. Edinburgh. *Joint Meeting with the Canadian Society of Anaesthetists.*

Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

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Examples of correct form of references
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JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294**: 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN. Pathogenic properties of invading micro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10: Data from the National Health Survey*, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUCHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

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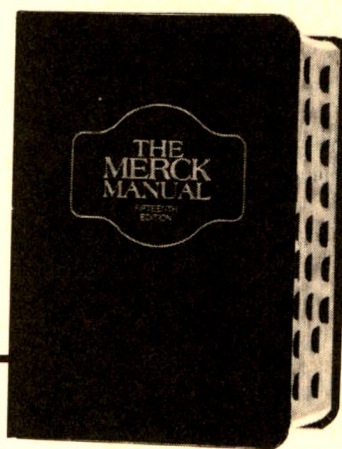
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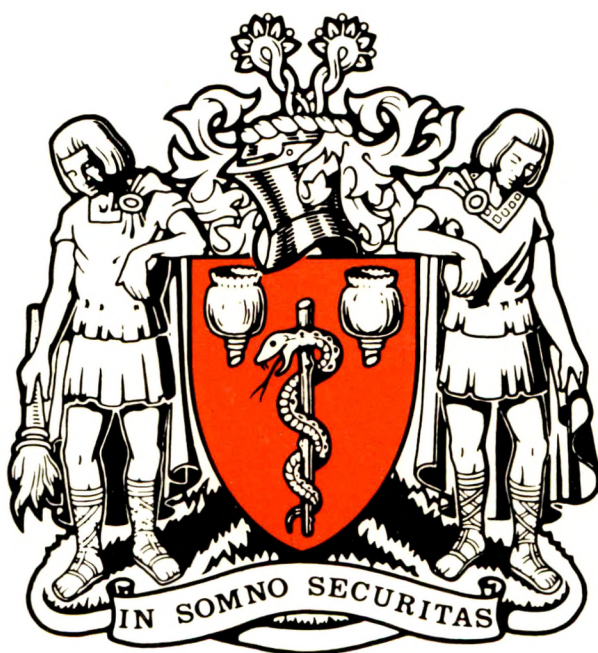
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Volume 43 Number 5 May 1988



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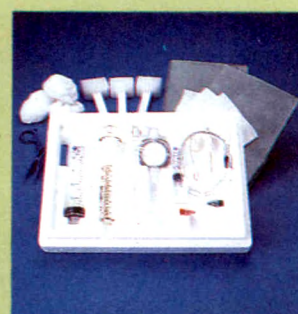
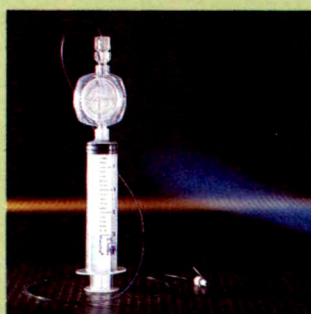
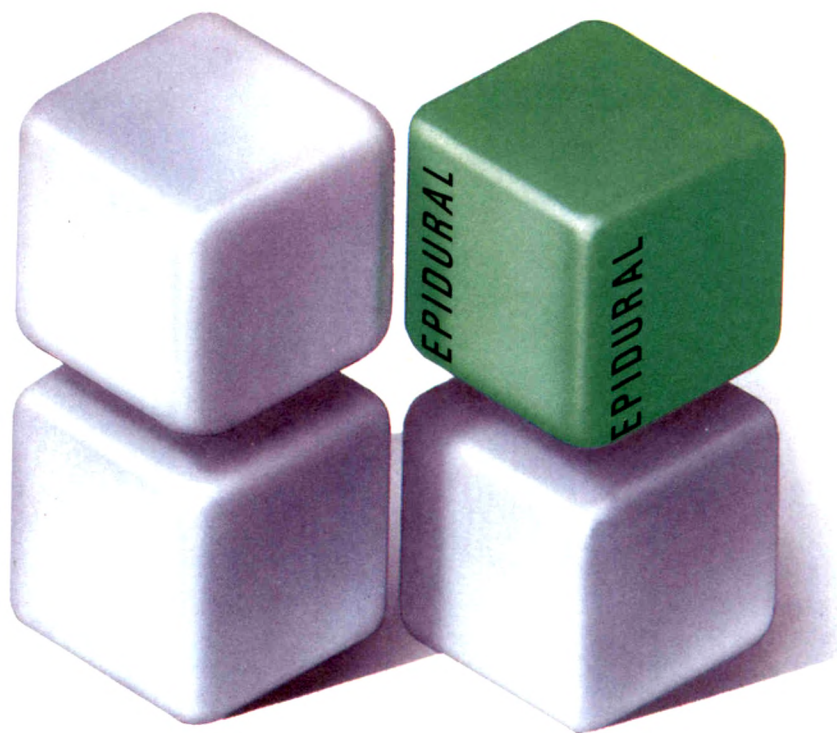
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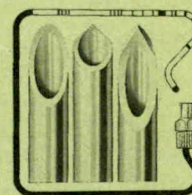


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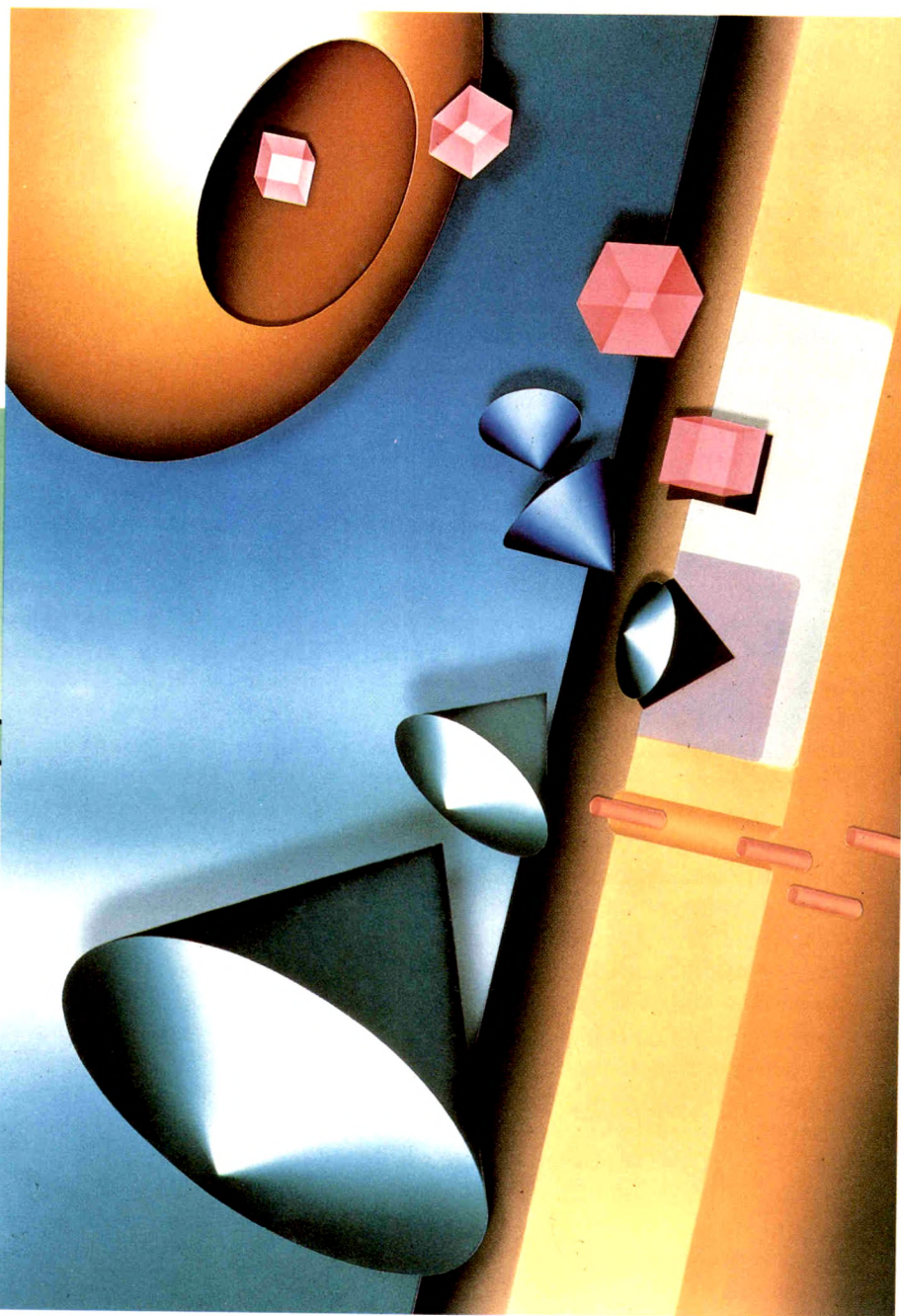
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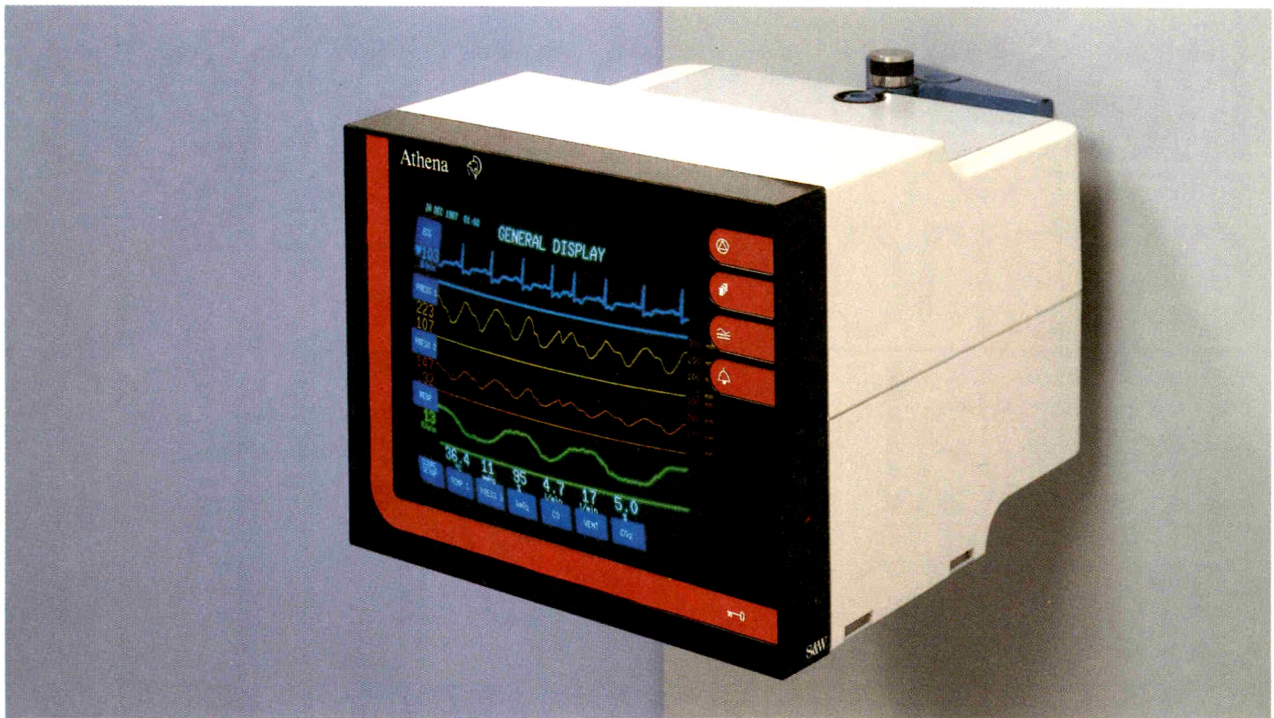
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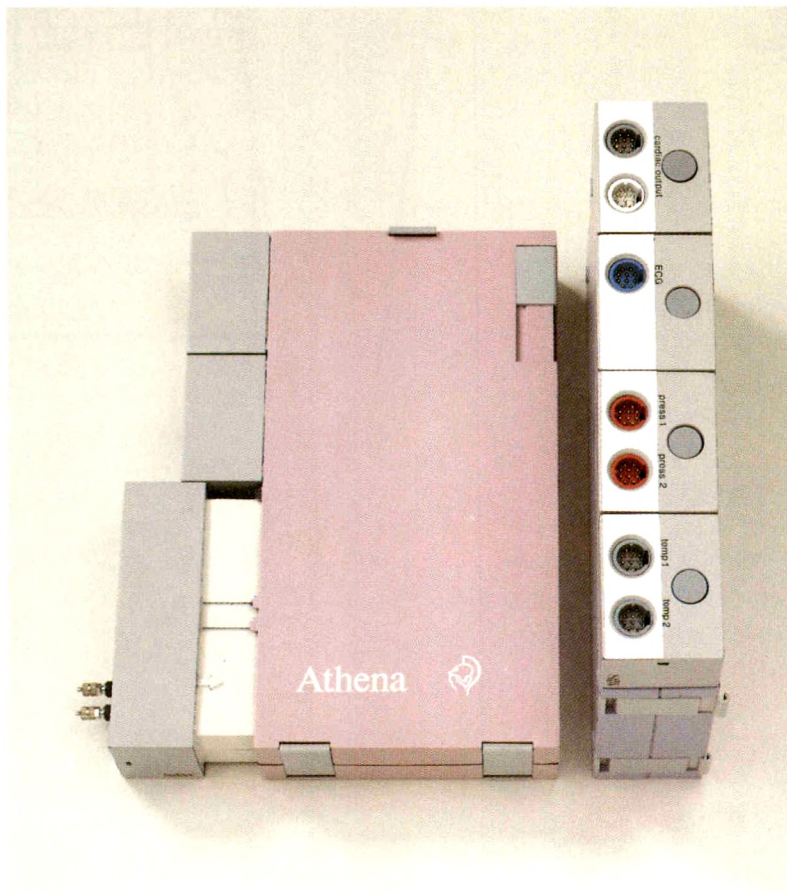
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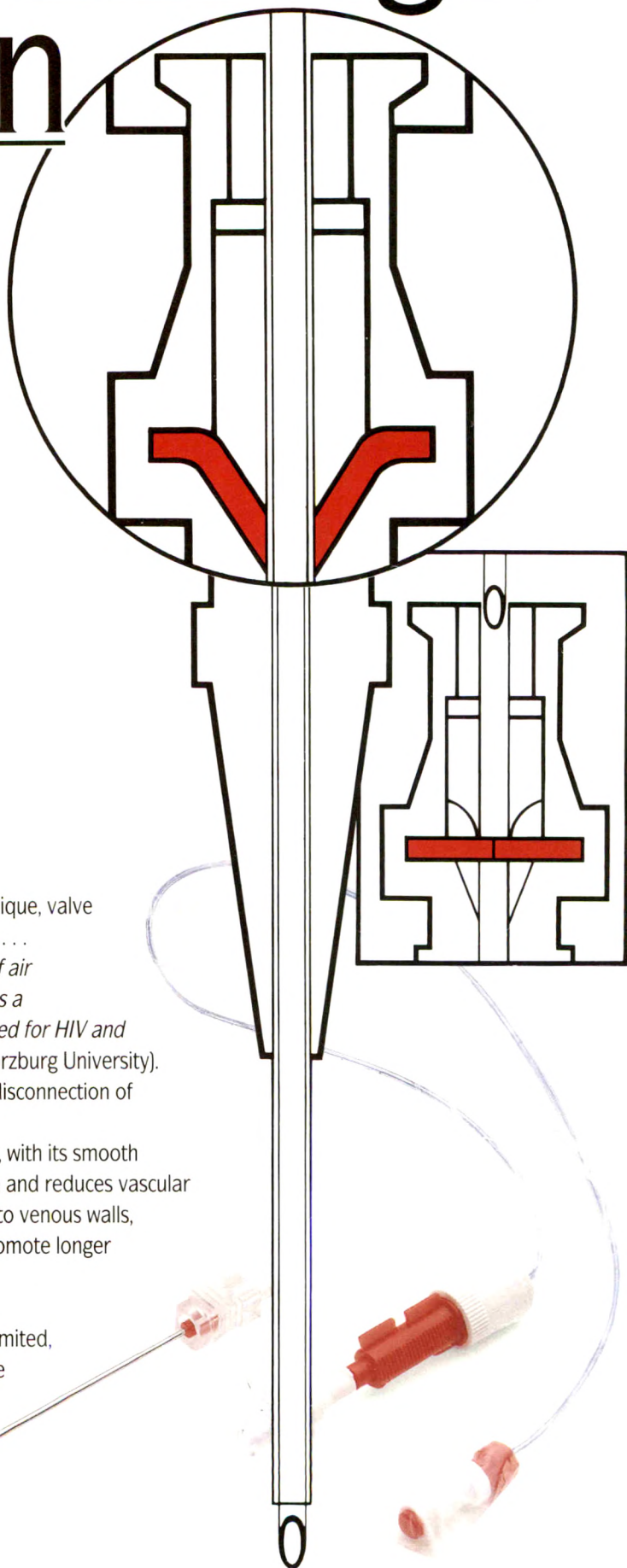
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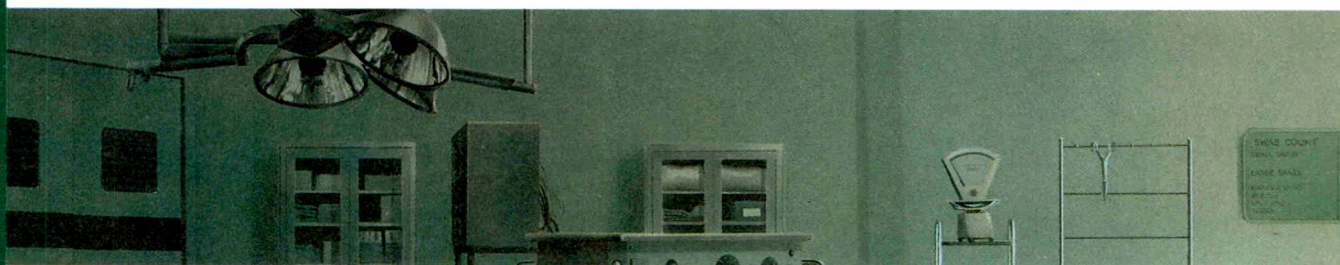
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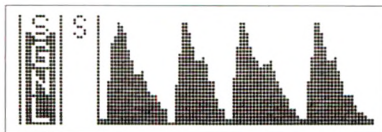
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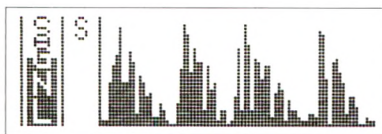
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"A well-designed oximeter should be able to detect power line frequency, compensate for background light flicker such as with fluorescent lamps, and display a true pulse waveform rather than bouncing dots."

Jeffrey B. Gross, M.D.
Associate Professor of Anesthesia
University of Pennsylvania,
Philadelphia, Pennsylvania



In the presence of a clean, physiological signal, the waveform is smooth, uniform and pulsatile in shape. The higher the signal strength indicator, the stronger the signal.



In the presence of interference, the waveform shows a noisy plethysmograph.

"In several of our studies of hypoxemia where it was important that the researchers and clinicians be blinded from the results, we found the waveform to be useful to distinguish real data from artifact."

Daniel B. Raemer, Ph.D.
Assistant Professor of
Anesthesia (Bioengineering)
Brigham and Women's Hospital
and Harvard Medical School
Boston, Massachusetts

"Observing the waveform is a vital aid to instantly rejecting artifact and is useful in providing extra data about the patient's cardiovascular system."

Richard Morris
M.B.B.S., F.F.A.R.C.S.
Staff Specialist
Department of Anaesthesia
and Intensive Care
Prince Henry Hospital
Little Bay, New South Wales
Australia

"Because the SaO₂ produced by the pulse oximeter is based on pulsatile absorbance of light, the pulsatile waveform is the essential quality control indicator."

William T. Cecil, R.R.T.
Coordinator
Respiratory Care Services
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"I feel secure that the information I am getting is based on a good pulse. I can trust the reading."

Gayle Miller, R.N.
Unit Administrator
Post-Anesthesia Care Unit
University Hospital
University of Colorado
Health Sciences Center
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"We would not consider purchase of a saturation monitor that did not have a waveform."

Anneke Meursing, M.D.
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¹Costarino AT, Davis DA, Keon TP: Falsely normal saturation reading with the pulse oximeter. *Anesthesiology* 67:830-831, 1987. ²Hanowell L, Eisele JH Jr, Downs D: Ambient light affects pulse oximeters, Correspondence. *Anesthesiology* 67:864-865, 1987. ³Swedlow DB, Running V, Feaster SJ: Correspondence. *Anesthesiology* 67:865, 1987. ⁴Block FE Jr: Interference in a Pulse Oximeter from a Fiberoptic Light Source. *Journal of Clinical Monitoring*, July 1987, pp 210-211. ⁵Brooks T, Paulus D, Winkle W: Infrared Heat Lamps Interfere with Pulse Oximeters. *Anesthesiology* 61:630, 1984.

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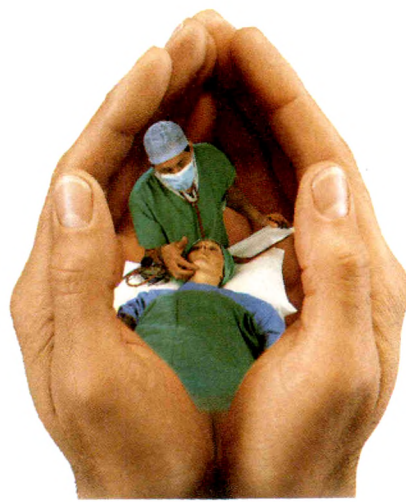
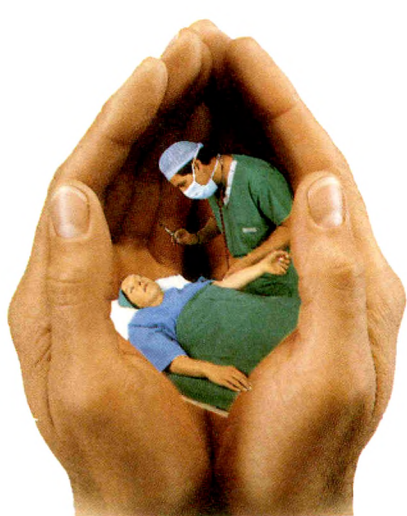
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Editorial

Anaesthesia, the clinician and the industrialist

One of the major criticisms levelled at the UK is our disappointing collective record for bringing innovations from concept to practical commercial reality. Many factors have been identified, not the least of which is the widely held view of some professions that commercial exploitation and personal gain are not acceptable goals of endeavour. It is fundamental that we all understand the message, reinforced by 1986 as Industry Year, that it is only by wealth creation that as a nation we can provide the financial resources necessary to fund the services we all believe essential to a civilized society. Therefore it is critical that industry and the medical profession work together effectively to bring to the marketplace new medical devices that satisfy the ever-demanding roles placed on them by advances in clinical practice, and to do so in as short a time as possible while high quality is maintained in the product.

The path from conception of the new idea for a medical product through to its commercial realisation is full of challenges and obstacles. One of the occasional obstacles to be surmounted is the mistrust felt by the clinician towards the industrialist. It is important not to flinch from accepting that an industrialist is indeed motivated by 'profit'. However, this goal should in no way reduce the personal, corporate and professional commitment to maintain a high standard of ethical conduct. Furthermore, no industrialist whose objective is to remain in business would set out to 'steal' a clinician's idea or indeed would deliberately contrive to undervalue the rewards to be shared with the clinician from the commercial exploitation of the idea.

Mutual trust comes from a clear understanding by both parties of their individual expectations and of the course that the collaboration will follow. It will be beneficial to both parties if the 'idea' can be the subject of a patent application before discussion; if this is not possible, then a clear written statement of the idea by the clinician will ensure that there is a record of it as it was presented to the industrialist. It is also a matter of good order which will lead to a better relationship, for the industrialist to provide the clinician with a statement of the terms under which he agrees to consider the idea, which the clinician will be asked to sign to acknowledge he appreciates those conditions. There are basically two approaches, and it is most important that both industry and clinicians should understand them.

First, a company may be prepared to sign a confidentiality agreement before seeing the inventor's information. That agreement will normally disclaim as nonconfidential, matter which is in the public domain, or known previously to the company, or supplied to it by another person having a right to do so. The company can find itself in great difficulties even with such disclaimers. Normally a clinician will approach a company with an idea which is directly in line with that company's business; an anesthetist does not turn to a manufacturer of urologicals in order to develop an anaesthetic device. There are very few genuinely original ideas, in the sense that most inventions are developments of existing technology, so the company may possess information which, if not identical, is similar to the clinician's. If the company signs a confidentiality agreement with a clinician *before* it is aware of the nature of the clinician's proposals, it can find itself in considerable difficulty in trying to distinguish the information it already possessed from that which the clinician gave it. More important, the company may bind itself to a clinician in respect of ideas or technology which were well within the company's capacity and may have been pursued by it independently.

Accordingly, some companies prefer the second approach, and ask to see a description of the invention (preferably in the form of a patent specification) to find out whether it interests them *before* entering into any obligations with the clinician. Clinicians should be aware that this is an approach used by a number of companies. It is not intended as way to cheat the clinician, but to preserve the company's ability to pursue its own research unfettered by obligations to others. The company's concern for its reputation, and its desire for the clinicians to have trust in it, are guarantees that this approach will not be abused. A confidentiality statement could include clauses covering the following: an undertaking to pursue reasonable steps to safeguard the confidentiality of the idea; a statement that if the idea submitted is of commercial value, the industrialist is prepared to negotiate for the rights of manufacture and sale of the idea; and finally a rider to the confidentiality clauses which would cover the situation where the idea is, or later becomes, publicly known or that the company is already aware of it, or made aware of it by a third party. Agreements covering confidentiality can run from a 20-line concise but effective statement to a document which runs to many pages. Written statements of mutual agreement are most desirable, but no agreement on its own can produce the trust necessary for effective collaboration; but they certainly assist.

Both parties will need to sit down and discuss the terms for a licence agreement at some stage during the collaboration; this is the formal mechanism which gives the industrialist the rights to manufacture and sell the idea, in return for financial recompense to the clinician. Licence agreements would contain clauses including: the granting of a licence to make, use and sell the idea, a definition of the idea by way of a patent number, a design registration or even know-how that has been involved and passed to the company, so that the idea can be commercialised; a statement of the term or life of the agreement and the date from which the agreement is effective; the nature of the financial recompense and the conditions which will enable the licence to be terminated.

An equitable financial arrangement from an industrialist's point of view require him to make a realistic judgment of the commercial value of the idea, having taken account of the risk involved. One of the factors in the assessment of commercial

risk is the strength of the patent. The better the idea is protected, the lower is its exposure to unfair competition once it is established in the marketplace. This, together with the usually large sums of money necessary for the development, manufacture and marketing of a new idea, assists in settling on an equitable royalty figure. It would certainly be normal practice to reduce royalty figures, compared with a protected idea if no protection exists for the idea. Or perhaps one royalty figure could be set for a period of, say, 5 years, to be followed by a lower royalty figure for a further number of years, which will be specified.

Large lump-sum payments for the rights of ideas are not usually accommodated by an industrialist because of the basic philosophy that if an idea succeeds, both parties should gain, whereas if it fails, neither should gain financially. Nevertheless there are often requests made for down payments on entering an agreement; if an industrialist agrees to such a clause he probably does so to underline his commitment to the project which acknowledges his inability to convey that this will usually be significant both in terms of equipment and of people necessary to take the idea from conception to production and sale. Consequently, the argument as to whether to opt for a lump-sum payment or royalties, normally sees the response to favour royalties; this in practice seems to be the fairer, because any collaboration should be viewed as a mutual sharing of risks and more often than not the industrialist puts in quite a large stake. If the product should succeed, both will benefit. Lump-sum payments are rather one-sided and could indeed result in an underestimation to the clinician, if the idea turns out to beat all expectations.

The use of a professional patent agent is desirable in order to maximise the effectiveness of the initial patent application. This may, however, create a financial barrier that the clinician inventor may not be prepared or able to overcome. Some companies may decide to fund the initial patent application on behalf of the inventor. If this turns out to be the case, such a decision would only occur if the company, at an early stage, thought the idea was worth speculative investment and also on the condition that they had the first option to the rights to the idea.

It is important to seek protection for an idea before its clinical use or its disclosure at conferences, because these actions constitute what is termed 'public disclosure'. Once an idea has been disclosed publicly, it is not possible to file a valid patent application; the major market where this does not apply is that of the United States of America, where there is a period of one year after disclosure in which to file a patent application.

The stages that most ideas pass through are: initial assessment and development; initial clinical trials; design/project review; multicentre and international clinical trials; final design specifications; provision of manufacturing tooling and facilities and finally the marketing and selling of the new idea. Thus there is a long, complex and expensive process through which a novel, even good idea has to pass before it can become a product.

If we look carefully at progress in medicine we will see that advances are made through evolutionary changes in procedures, equipment and devices, and quantum leaps, both of which are seeded by real clinical needs and satisfied by state of the art product design and technological developments. Clinicians have responsibilities that go further than those for their current patients; the prospects for improving their future care will depend on good communication between industry and the profession. This is a challenge to both parties and like all relationships if it starts well with both parties working together it has a good chance of success. This success leads to an increase in the nation's wealth.

Technical Director,
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P.J. BRAND

Editorial notices

Submission of manuscripts

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biomedical journals* (British Medical Journal 1979; 1: 532-5). Details will be found in the Notice of Contributors To *Anaesthesia* at the end of this issue,

Anaesthesia News

Copy for *Anaesthesia News* should be sent to the Editor as and when it becomes available. It is hoped that publication will occur within 2 months of receipt.

Resuscitation in late pregnancy

G. A. D. REES AND B. A. WILLIS

Summary

This paper considers cardiopulmonary resuscitation in obstetric patients at term and the influence of aortocaval compression on the outcome. The maximum chest compression force produced by eight physicians was measured as a function of angle of inclination using an inclined plane. The compression force at an angle of 27° is 80% of that in the supine position and the Cardiff resuscitation wedge, designed to prevent aortocaval compression, is described with this inclination. Midwives' expertise in basic life support 6 months after instruction was assessed using a manikin simulator. The majority had acquired errors in external chest compression and mouth to mouth ventilation. These were corrected by additional tuition. Resuscitation of the manikin on the Cardiff wedge was found to be as efficient as in the supine position.

Key words

Complications; heart, arrest.

Equipment; resuscitation wedge.

Cardiac arrest in late pregnancy may be estimated to occur once in 30 000 pregnancies¹ and survival after such an event is exceptional² unless it occurs during general anaesthesia. There are factors in addition to speed of response and expertise in cardiopulmonary resuscitation (CPR) by medical and midwifery staff, which weigh the balance against the survival of a pregnant patient. These include the cardiotoxic effects of bupivacaine³ and aortocaval occlusion. Bupivacaine cardiotoxicity implies unrecognised injection of local anaesthetic into an epidural vein although deaths have occurred following intrathecal injection. Aortocaval occlusion by the gravid uterus is well recognised in the obstetric patient near term⁴ and, experimentally, resuscitation of dogs is found to be more difficult when the inferior vena cava is partly occluded.⁵

Marx⁶ reviewed five obstetric cases in whom resuscitation was required for more than 10 minutes following inadvertent intravenous injection of bupivacaine. The three patients who underwent immediate Caesarean section (so removing aortocaval occlusion) survived with no neurological deficit whereas those in whom delivery was delayed suffered irreversible brain damage.

There has also been a report⁷ of a postmortem Caesarean section when maternal resuscitation was thought to have failed, following which resuscitation of mother and child was successful and there has recently been a similar case in Cardiff. Lindsay and Hanson⁸ report a successful resuscitation after Caesarean section in a preterm gravid patient who had sustained cardiac arrest at home. Drawing

conclusions from such small numbers is unwise but the removal of aortocaval compression by delivery is probably one of the major factors determining survival.

The implication must be that conventional CPR with the patient in the supine position is unlikely to succeed in late pregnancy since the heart is poorly supplied due to lack of venous return. The present study therefore had two main objectives: first, to determine whether an effective chest compression force could be applied with the patient inclined so that aortocaval compression would be prevented; the production of the Cardiff resuscitation wedge was a natural consequence of this part of the study; and second, to assess the level of expertise in basic life support of midwifery staff who had received instruction 6 months previously in order that recommendations might be made about such training.

Methods

The efficacy of resuscitation with the patient at various angles of inclination was assessed by use of the arrangements shown in Fig. 1. A calibrated force transducer was fitted on a plane capable of inclination between 0° (supine) and 90° (full lateral). The height of the transducer above the ground was 30 cm, which is the approximate height of the chest of a patient during resuscitation on the ground. The maximum possible resuscitative force measured by the force transducer was expressed as a function of the angle of inclination, θ . The exercise was performed by seven anaesthetists with experience which ranged from 5-20

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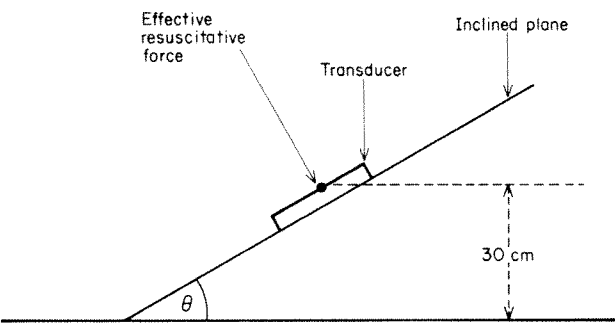


Fig. 1. Experimental arrangement used to measure effective resuscitative force as a function of angle of inclination, θ .

Table 1. Resuscitation force as a function of angle of inclination, θ . Values expressed as mean (SD).

Angle of inclination, θ	Maximum resuscitative force as percentage of body weight	
	Hands in CPR position	Hands juxtaposition
0°	66.7 (6.5)	67.5 (8.2)
27°	53.3 (5.5)	54.6 (6.3)
32°	46.4 (3.9)	48.1 (4.3)
49°	41.5 (3.5)	40.6 (3.2)
90°	36.3 (5.4)	35.1 (5.7)

years, and by one senior registrar in cardiology. Their resuscitative force for each angle of inclination, was expressed as a percentage of their body weight. The results are illustrated in Fig. 2 and Table 1. Measurements were made with the resuscitator's hands overlapping (as in CPR) and also with the hands juxtapositioned.

Results

The maximum possible resuscitative force decreased as the angle of inclination of the plane increased, from 67% of

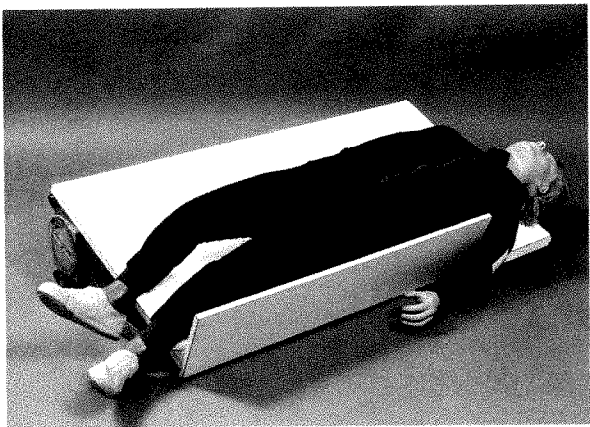


Fig. 3. The Cardiff resuscitation wedge with the Resusci Anne Manikin in position.

body weight in the supine position ($\theta = 0^\circ$) to 36% in the full lateral ($\theta = 90^\circ$). There was no significant difference in the data obtained with the resuscitator's hands in the CPR position or juxtapositioned. There was no tendency at an angle $\theta < 30^\circ$ for the manikin, or human volunteer placed on the inclined plane, to slide or roll from the inclined plane. $\theta = 27^\circ$ corresponded to an ability to apply a resuscitative force of 55% of the body weight of the resuscitator, that is 80% of the force which could be applied in the supine position. The Cardiff resuscitation wedge (Fig. 3) was manufactured at St David's Hospital, Cardiff as a result of these measurements.

The Cardiff resuscitation wedge

The wedge has a stout wooden frame; all external surfaces are laminated for easy cleaning and it is fitted with castors on its side so that it may be transported easily to the site of an arrest. Other features include a fixed side piece to

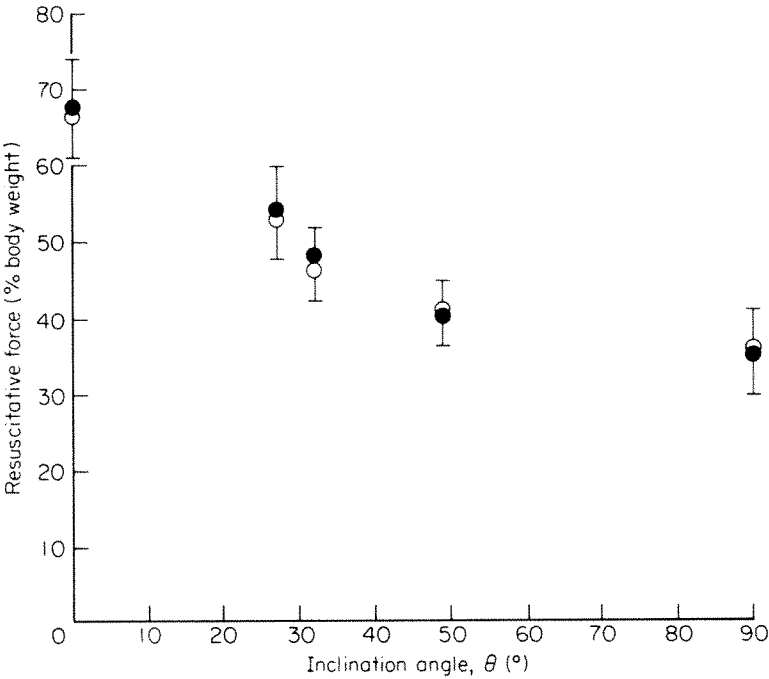


Fig. 2. Mean (SD) effective resuscitative force as a function of angle of inclination, θ . ●, Hands apart; ○, hands in CPR position.

maintain the patient on the wedge but which allows the patient's arm to lie off the wedge so that a site is available for venous access. The length of the wedge is 100 cm: this corresponds approximately to the distance from the cervical spine to below the ischial tuberosities, and gives good access to the obstetric team below and the anaesthetist above, while the resuscitator who applies external chest compression kneels alongside. The absence of a fixed head support means that the wedge is physically smaller, and therefore easily portable. The patient's head may be positioned as necessary for tracheal intubation, or expired air ventilation, with a pillow under the head. The neck is accessible for cannulation of the internal jugular veins.

Training of personnel

The efficacy of bystander resuscitation is increasingly recognised⁹ and every mother in labour has a midwife standing by to recognise an arrest and start resuscitation immediately. In-service training of all midwifery staff in Cardiff is carried out by anaesthetic senior registrars and consultants. In 1985, 74 midwives underwent successful training in basic life support (using a Recording Resusci Anne Manikin) and their skills (which fortunately they had no previous opportunity to practise) were checked 6 months later.

We found at the 6-monthly check on 24 of these midwives selected at random, that chest compression was applied correctly to the supine manikin by only four of them (16%). The main faults (Table 2) were incorrect hand position and inappropriate compression force and rate and rhythm of compression. Fifty per cent were able to perform mouth to mouth expired air ventilation satisfactorily but correct head positioning was as difficult as ventilation. Ten minutes of tuition and practice restored their ability to perform both these tasks, which confirmed that short periods of instruc-

tion at regular intervals are necessary to maintain resuscitative expertise.¹⁰

The results after tuition are summarised in Table 3. It is worth noting that three of the 24 were still unable to perform satisfactory chest compression and five were unable to perform satisfactory mouth to mouth expired air ventilation on the manikin at this time. There was no significant change in these figures (Table 3) when the manikin was put on the Cardiff resuscitation wedge inclined at 27° and the midwives given the opportunity of resuscitation.

Conclusions

The resuscitation of a pregnant patient at term is a rare event and is unlikely to be successful unless aortocaval compression by the gravid uterus is relieved. It is evident from the present inclined plane measurements that it is a practical proposition to apply chest compression forces with the patient inclined at angles of less than 30°. There is a tendency for the resuscitatee to roll or slide off the inclined plane at angles greater than this. It is obvious that, in order to maintain their resuscitative skills, midwives should have frequent opportunities to practise on a simulator in order to correct acquired errors. It is also apparent from this study that effective resuscitation by midwives may be performed with the patient in the inclined position.

The inclined plane resuscitation wedge allows access to the patient by obstetricians and anaesthetists if surgical intervention is required. It is essential that the bystanders are capable of effective resuscitation techniques and have the necessary equipment if the tragedy of a cardiac arrest in the obstetric patient at term is to be averted.

References

1. DEPARTMENT OF HEALTH AND SOCIAL SECURITY. *Report on confidential inquiries into maternal deaths in England and Wales 1976-78, 1979-81*. London: HMSO, 1982, 1986.
2. STOKES IM, EVANS J, STONE M. Myocardial infarction and cardiac arrest in the second trimester followed by assisted vaginal delivery under epidural analgesia at 38 weeks gestation. Case report. *British Journal of Obstetrics and Gynaecology* 1984; **91**: 197-8.
3. REIZ S, NATH S. Cardiotoxicity of local anaesthetic agents. *British Journal of Anaesthesia* 1986; **58**: 736-46.
4. KERR MG, SCOTT DB, SAMUEL E. Studies of the inferior vena cava in late pregnancy. *British Medical Journal* 1964; **1**: 532-3.
5. KASTEN GW, MARTIN ST. Resuscitation from bupivacaine-induced cardiovascular toxicity during partial inferior vena cava occlusion. *Anesthesia and Analgesia* 1986; **65**: 341-4.
6. MARX GF. Cardiopulmonary resuscitation of late-pregnant women. *Anesthesiology* 1982; **56**: 156.
7. DEPACE NL, BETESH JS, KOTLER MN. 'Postmortem' cesarean section with recovery of both mother and offspring. *Journal of the American Medical Association* 1982; **248**: 971-3.
8. LINDSAY SL, HANSON GC. Cardiac arrest in near-term pregnancy. *Anaesthesia* 1987; **42**: 1074-7.
9. RITTER G, WOLFE RA, GOLDSTEIN S, LANDIS JR, VASU CM, ACHESON A, LEIGHTON R, MEDENDORP SV. The effect of bystander CPR on survival of out-of-hospital cardiac arrest victims. *American Heart Journal* 1985; **110**: 932-7.
10. Standards and guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiac care (ECC). *Journal of the American Medical Association* 1986; **255**: 2905-14.

Table 2. Basic life support assessment of midwifery staff ($n = 24$) using a manikin, 6 months after initial instruction.

	Satisfactory	Unsatisfactory
External chest compression	4	20
Hand position	4	20
Compression force	15	9
Compression rate	17	7
Compression rhythm	22	2
Mouth to mouth ventilation	12	12
Head position	12	12
Ventilation	12	12

Table 3. Basic life support assessment of midwifery staff ($n = 24$) after additional tuition.

	Satisfactory	Unsatisfactory
External chest compression (supine)	21	3
External chest compression (27°)	21	3
Mouth to mouth ventilation (supine)	19	5
Mouth to mouth ventilation (27°)	20	4

Propofol for induction of anaesthesia in children

A comparison with thiopentone and halothane inhalational induction

N. S. MORTON, M. WEE, G. CHRISTIE, I. G. GRAY AND I. S. GRANT

Summary

The induction characteristics, dosage requirements, cardiovascular and respiratory effects of propofol with added lignocaine were compared with those of thiopentone and halothane inhalational induction in two groups of children aged 1–5 years and 5–10 years. Propofol induction produced significantly greater decreases in blood pressure, particularly in the 1–5-year age group. Heart rate was maintained well with all three induction techniques. Pain on injection into a vein on the dorsum of the hand was significantly more common with propofol despite the addition of lignocaine. However, this was mild in the majority of children and did not interfere with the induction of anaesthesia. The incidence of respiratory depression and other adverse effects was low with all three induction methods. The mean induction doses of both intravenous agents were greater in the 1–5-year age group. The ratio of thiopentone to propofol dose was approximately 2.5:1 in both age groups. The high incidence of pain on injection with propofol may prove to be a significant drawback to its otherwise satisfactory use in children.

Key words

Anaesthetics, intravenous; propofol, thiopentone.

Anaesthetics, volatile; halothane.

Induction of anaesthesia with halothane in children has been shown to cause a dose-dependent decrease in blood pressure which is related to depression of myocardial contractility and decrease in heart rate, with little change in systemic vascular resistance.^{1–6} The introduction of isoflurane provided the impetus for further comparative studies which demonstrated that isoflurane produces a similar decrease in blood pressure but due to a decrease in systemic vascular resistance rather than to myocardial depression. Respiratory side effects are more common.^{7–9} Thiopentone appears to produce a dose-related reduction in blood pressure associated with an increase in heart rate.^{2,10–12} Propofol has been investigated extensively for induction of anaesthesia in adults but experience with this new agent in children is limited.¹³

The aims of this study were to record the induction characteristics, dosage requirements, and cardiovascular and respiratory effects of propofol in comparison with thiopentone and halothane inhalational induction in two groups of children aged 1–5 years and 5–10 years.

Patients and methods

Local hospital ethical committee approval was given for this study. All parents and children were interviewed on the day before surgery to explain the study and to ascertain

their preference for an intravenous or an inhalational induction of anaesthesia. The children in the intravenous groups were then allocated randomly to receive propofol or thiopentone. Informed parental consent was obtained. Thiopentone induction was used if the parents did not wish their child to have propofol.

Two groups of 30 children, aged 1–5 years and 5–10 years were studied. Only ASA grade 1 or 2 patients who presented for elective, inpatient general surgical procedures were included in the study. Children were specifically excluded if there was a history of asthma or allergies, previous adverse experience with general anaesthesia, halothane anaesthesia within the last month, hepatic, renal, respiratory, cardiac, haematological or metabolic disease, or if mentally retarded. The child was withdrawn from the study if pre-induction values of blood pressure and heart rate could not be obtained or if venous access was not readily achieved.

Premedication consisted of diazepam syrup 0.25 mg/kg and droperidol syrup 0.25 mg/kg orally, given 2 hours pre-operatively. All children had an intravenous cannula (Wallace Y-Can, 23 gauge) sited on the dorsum of the hand. This was done 5 minutes after the child was anaesthetised in the halothane induction group.

Pre-induction values of blood pressure and heart rate were obtained using a Dinamap 845 XT monitor and an

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appropriate cuff placed on the arm opposite to the intravenous cannula. The patient was allowed to settle after cannulation before pre-induction readings were taken in the intravenous induction groups. Further readings of blood pressure and heart rate were taken at one-minute intervals from the start of the induction sequence.

Lignocaine 10 mg was added to each 200-mg ampoule of propofol. Either propofol 2 mg/kg or thiopentone 5 mg/kg was injected over 10 seconds. Further induction agent was titrated after waiting for 10 seconds, at half the initial rate until the patient was able to tolerate the facemask. Thus, for each agent, an initial bolus was given at a rate of 0.02 ml/kg second for 10 seconds, followed by a pause for 10 seconds. Further induction agent was then given if required, at a rate of 0.01 ml/kg second until toleration of the facemask. The total dose of drug used was recorded.

Thereafter, anaesthesia was maintained with nitrous oxide 67% in oxygen with halothane 1–3% delivered by a Mapleson F system in the 1–5-year age group and by a Bain system in the 5–10-year age group. Fresh gas flow (FGF) was set according to the formula: FGF (litres/minute) = $2 \times \sqrt{\text{body weight (kg)}}$.

Delivery of this gas mixture to the child during induction in the halothane group, was via the angle-piece of the anaesthetic system and the cupped hand of the anaesthetist. The halothane concentration was increased by 0.5% increments from the starting level of 1% up to a maximum of 3%. The mask was placed on the face as soon as the child closed his/her eyes.

An appropriate local or regional nerve block was performed in all patients at the conclusion of the 5-minute induction period.

Any adverse effects and their duration were noted in addition to haemodynamic data and dosage requirements. Pain on injection was assessed in four categories: none; mild (grimace only); moderate (crying); and severe (crying and withdrawal of arm). Involuntary movements and respiratory side effects, such as apnoea, breath holding, hiccoughs, coughing and laryngospasm, were noted. A record was made of any intra-operative complications, including bradycardia which required treatment with atropine, and of any postoperative problems such as vomiting. Venous sequelae were assessed at the postoperative visit. No attempt was made to evaluate postoperative recovery in view of the variety of surgical procedures and analgesic techniques performed.

Statistical analysis of the data was performed using Student's *t*-test and the Chi-squared test with Yates' correction (for small numbers) where appropriate.

Results

The three induction groups were well matched for age, weight and pre-induction blood pressure and heart rate (Tables 1 to 4). The haemodynamic data after induction are shown in Tables 3 and 4 (see next page), and summarised in the graphs of mean blood pressure and heart rate (Figs 1 and 2).

Propofol induction produced a significant decrease from pre-induction values of systolic, mean and diastolic blood pressure in both age groups. This decrease was greater than those that followed halothane or thiopentone induction, irrespective of age.

Heart rate was maintained well with all induction tech-

Table 1. Patient data for children aged 1–5 years, expressed as mean (SEM).

	Halothane (n = 10)	Thiopentone (n = 10)	Propofol (n = 10)
Age, months	36.3 (5.7)	40.2 (4.2)	36.8 (3.2)
Sex, M:F	10:0	9:1	10:0
Weight, kg	13.5 (1.0)	15.0 (0.8)	14.3 (0.7)

Table 2. Patient data for children aged 5–10 years, expressed as mean (SEM).

	Halothane (n = 10)	Thiopentone (n = 10)	Propofol (n = 10)
Age, months	82.8 (6.0)	86.0 (6.9)	76.0 (3.5)
Sex, M:F	8:2	10:0	10:0
Weight, kg	22.6 (1.6)	25.2 (2.0)	21.8 (1.8)

Table 5. Incidences of adverse effects in age group 1–5 years.

	Halothane (n = 10)	Thiopentone (n = 10)	Propofol (n = 10)
Pain on injection	0	0	6*†
Apnoea	0	4‡	1**
Breath holding	0	0	0
Hiccoughs	0	1§	0
Coughing	0	0	0
Laryngospasm	0	0	0
Involuntary movements	0	0	1¶
Vomiting	0	0	0
Postoperative vomiting	0	0	0
Dysrhythmias	0	0	0

* $p < 0.05$.

† Mild 4, moderate 1, severe 1.

‡ Durations 5, 7, 10 and 20 seconds.

§ Duration 15 seconds.

¶ Duration 20 seconds.

** Duration 45 seconds.

Table 6. Incidences of adverse effects in age group 5–10 years.

	Halothane (n = 10)	Thiopentone (n = 10)	Propofol (n = 10)
Pain on injection	0	0	5*†
Apnoea	0	1‡	2§
Breath holding	0	1¶	0
Hiccoughs	0	0	0
Coughing	0	1¶	0
Laryngospasm	0	0	0
Involuntary movements	0	0	1**
Vomiting	0	0	0
Postoperative vomiting	0	0	0
Dysrhythmias	0	0	0

* $p < 0.05$.

† Mild 4, moderate 1.

‡ Duration 20 seconds.

§ Duration 15 and 20 seconds.

¶ Duration 5 seconds.

** Duration 10 seconds.

niques. Thiopentone and propofol both tended to produce an initial increase in heart rate which settled more quickly in the propofol groups.

Pain on injection (Tables 5 and 6) was significantly more frequent with propofol despite the addition of lignocaine 10 mg to each 200-mg ampoule. This was scored as mild in the majority (8 out of 11) who complained of pain, and did not interfere with the induction of anaesthesia. Induction with propofol was otherwise smooth in the majority of patients in both age groups. Both thiopentone and propofol produced a higher incidence of adverse effects than halothane induction. Apnoea occurred more commonly with thiopentone (5/20) but was transient (5–20 seconds). Pro-

Table 3. Blood pressure and heart rate for age group 1–5 years, expressed as mean (SEM).

Time postinduction (minutes)											
Pre-induction			2			3			4		
H	T	P	H	T	P	H	T	P	H	T	P
Systolic blood pressure, mmHg	112.7 (3.4)	118.6 (4.0)	110.9 (3.2)	122.5 (5.8)	123.0 (9.2)	105.8 (4.9)	110.4 (3.4)	95.7*† (3.4)	99.3* (3.9)	103.4* (4.1)	91.6*† (3.2)
Mean blood pressure, mmHg	84.1 (3.7)	81.7 (5.1)	79.6 (4.0)	91.7 (5.9)	93.7 (9.8)	77.7 (3.0)	81.1 (4.0)	76.2 (5.4)	69.6* (3.4)	72.1 (2.6)	61.0*† (3.2)
Diastolic blood pressure, mmHg	71.2 (3.7)	63.0 (3.3)	65.1 (4.1)	74.7 (6.3)	75.3 (9.5)	59.5* (2.6)	64.5 (3.4)	56.6 (4.1)	53.8* (3.4)	51.1* (2.3)	44.6*† (2.1)
Heart rate, beats/minute	116.2 (6.3)	113.2 (6.0)	108.2† (6.5)	127.5† (4.1)	130.7† (8.8)	112.9 (7.0)	126.5 (5.3)	104.2† (8.2)	109.0† (5.5)	114.9 (2.7)	103.0 (6.5)

H = halothane; T = thiopentone; P = propofol. * Significant difference from pre-induction value ($p < 0.05$). † Significant difference from halothane group. ‡ Significant difference from thiopentone group.

Table 4. Blood pressure and heart rate for age group 5–10 years, expressed as mean (SEM).

Time postinduction (minutes)											
Pre-induction			2			3			4		
H	T	P	H	T	P	H	T	P	H	T	P
Systolic blood pressure, mmHg	105.0 (1.9)	107.6 (4.8)	105.1 (2.6)	116.7 (5.1)	109.6 (4.1)	100.0† (2.2)	112.7† (3.9)	103.0 (3.6)	97.6*† (2.0)	107.4† (3.7)	96.0*† (2.7)
Mean blood pressure, mmHg	75.0 (3.6)	76.9 (3.3)	75.3 (3.8)	84.8 (4.7)	78.0 (3.4)	73.0 (2.9)	80.4 (4.6)	73.7 (3.8)	67.9† (1.8)	77.6† (3.8)	67.6*† (2.6)
Diastolic blood pressure, mmHg	63.5 (3.9)	60.5 (4.0)	61.4 (2.9)	67.6 (4.8)	61.3 (4.0)	56.3 (1.8)	61.8 (3.7)	55.4 (2.8)	53.9* (1.6)	56.5 (4.1)	47.7*† (1.6)
Heart rate, beats/minute	83.1 (2.6)	84.8 (3.0)	85.9 (5.7)	95.3 (4.6)	92.3 (5.9)	87.0† (6.0)	106.7*† (2.1)	97.0† (3.5)	86.2† (3.3)	101.3*† (3.8)	93.9 (3.6)

H = halothane; T = thiopentone; P = propofol. * Significant difference from pre-induction value ($p < 0.05$). † Significant difference from halothane group. ‡ Significant difference from thiopentone group.

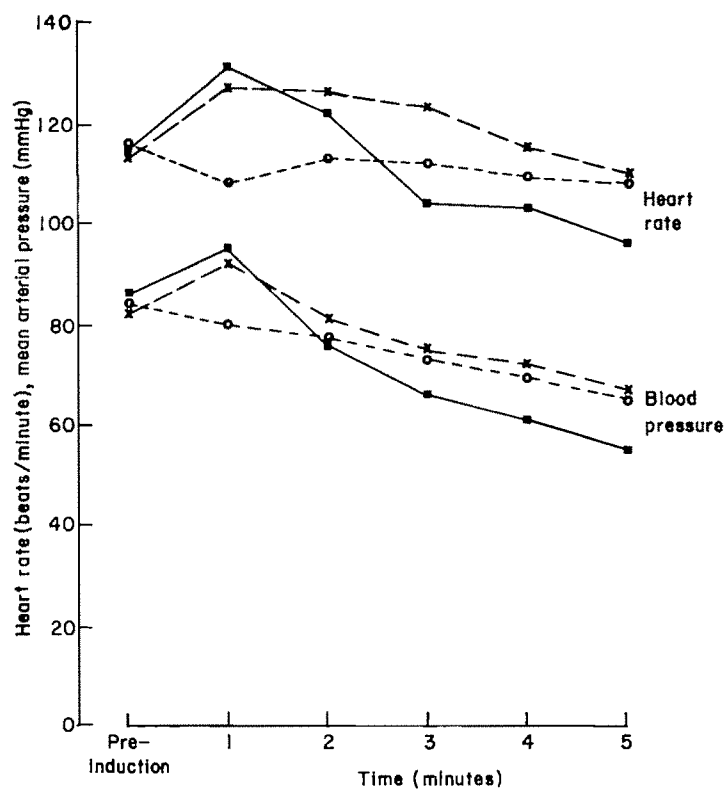


Fig. 1. Mean heart rate and arterial pressure, age group 1-5 years. Refer to Table 3 for significance of changes from pre-induction values and of differences between groups. —, Propofol; ----, halothane; ---, thiopentone.

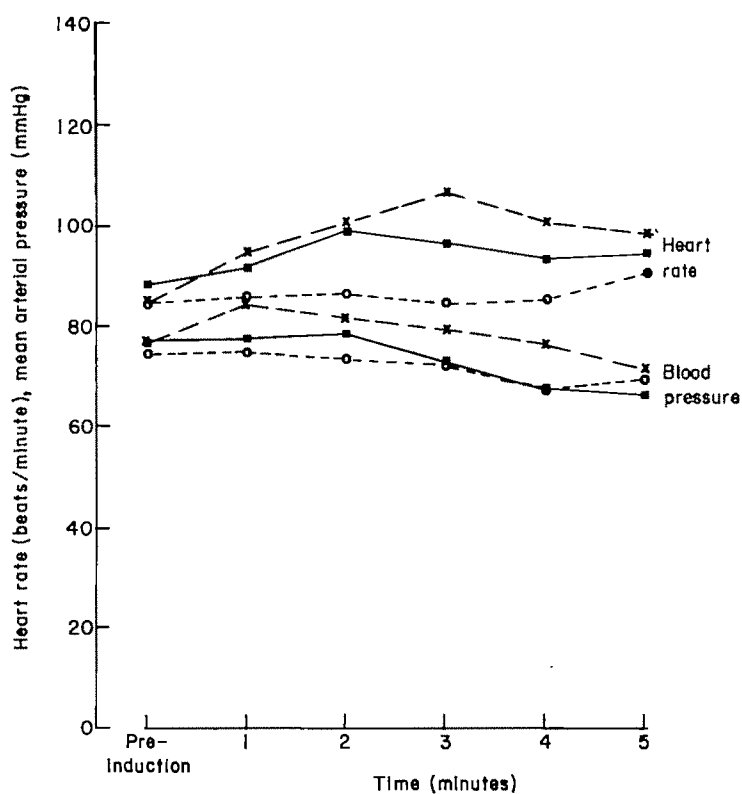


Fig. 2. Mean heart rate and arterial pressure, age group 5-10 years. Refer to Table 4 for significance of changes from pre-induction values and of differences between groups. —, Propofol; ----, halothane; ---, thiopentone.



Table 7. Induction dose requirements and times.

Thiopentone (n = 20)				Propofol (n = 20)				
Dose (mg/kg)		Number given additional doses	Mean (SEM) time to tolerate facemask, seconds	Dose (mg/kg)		Number given additional doses	Mean (SEM) time to tolerate facemask, seconds	Ratio thiopentone: propofol
Mean (SEM)	Range			Mean (SEM)	Range			
<i>Age group 1-5 years</i>								
5.65 (0.19)	5.00- 6.58	7	19.5 (3.8)	2.28 (0.08)	2.00- 2.78	9	21.4 (2.7)	2.48:1
<i>Age group 5-10 years</i>								
5.43 (0.27)	5.00- 7.60	4	19.8 (5.2)	2.10 (0.05)	2.00- 2.40	4	19.2 (2.3)	2.61:1

propofol produced apnoea in only three out of 20 patients but this lasted for 45 seconds in one patient in the 1-5-year age group. Hiccoughs, breath holding and coughing occurred only with thiopentone induction (one case of each) while involuntary movements occurred only with propofol (one case in each age group).

None of these adverse effects interfered significantly with the induction of anaesthesia. No instances of laryngospasm or vomiting occurred during the study and no serious dysrhythmias were seen, although two patients who received propofol (one in each age group) required atropine intra-operatively for sinus bradycardia associated with surgical stimulation. One patient in the halothane induction group, age 1-5 years, required atropine intra-operatively.

The induction dosage requirements (Table 7) indicate a thiopentone:propofol ratio of approximately 2.5:1 in both age groups, using toleration of the facemask as the endpoint. A greater number of patients in the 1-5-year age group required more than the initial dose of thiopentone or propofol (7/10 and 9/10, respectively) and the mean dose was higher with both agents in the younger age group. The mean induction time was similar for thiopentone and propofol (Table 7) in both age groups.

There were no adverse postoperative sequelae in any of the patients in the study.

Discussion

Induction of anaesthesia with propofol was noticeably smooth and free from respiratory side effects in both age groups but was associated with a significantly greater decrease in blood pressure than either thiopentone or halothane inhalational induction. However, this decrease at 5 minutes of approximately 25% from pre-induction levels was clinically acceptable and of the same order of magnitude as reported previously in 8-14-year-old children.¹³ The decrease in blood pressure became statistically significant 3 minutes after induction, by which time the patients were breathing halothane 3%, and this is likely to have contributed to the decrease. Our findings with regard to haemodynamic changes after thiopentone and halothane are consistent with the known effects of both agents.¹⁻¹²

The high incidence of pain on injection into a vein on the dorsum of the hand occurred despite the addition of lignocaine as recommended by Redfern *et al.*¹⁴ They found in adults that the incidence of pain on injection into a vein on the dorsum of the hand could be reduced to less than 4% by the addition of lignocaine 0.5 mg to each 9.5 mg of propofol emulsion. This was a significantly lower incidence than after plain propofol, pre-injection of lignocaine or any

of the other suggested pretreatment regimens.¹⁵⁻¹⁸ It is important that the lignocaine is added immediately prior to use, because efficacy declines after 30 minutes; this may be due to movement of the lignocaine into the lipid phase. The emulsion may also start to destabilise after this time,¹⁶ and the possibility of a chemical interaction has been noted.¹⁹

An alternative method to reduce the incidence of pain is to use the antecubital veins; propofol has been shown to cause no tissue damage after perivascular and intra-arterial injection.²⁰ However, this still produces an incidence of severe pain on injection in children of at least 5%.¹³ Further new initiatives are needed in this area.

The mean dose requirements for propofol in the present study were 2.28 mg/kg (range 2.00-2.78) for the 1-5-year group and 2.10 mg/kg (range 2.00-2.40) for the 5-10-year group; these values are similar to those found in premedicated adults. We used a titration sequence which was very similar to that used in general clinical practice. Toleration of the facemask as an endpoint for satisfactory induction has been commended previously as the best clinical indicator of induction in children.¹⁰ Loss of the eyelid reflex is not a consistent endpoint for induction with propofol.²¹

The mean dose requirements for thiopentone were 5.65 mg/kg (range 5.00-6.58) in the 1-5-year age group and 5.48 mg/kg (range 5.00-7.60) in the 5-10-year age group.³ The textbook dose recommendation for children is 2-5 mg/kg but it was only as recently as 1981 that the first prospective randomised study of dose requirements was published.¹⁰ This showed that unpremedicated, healthy children between the ages of 5 and 15 years invariably require 5-6 mg/kg to ensure an adequate depth of anaesthesia for a smooth transition to general inhalational anaesthesia. Our dose ratio of 2.5:1 for thiopentone to propofol is slightly higher than that found previously in studies of premedicated adults.

Propofol induction, despite its otherwise smooth characteristics and acceptable cardiovascular effects, is associated with an unacceptably high incidence of pain on injection which may limit its everyday use in paediatric anaesthesia.

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References

1. MCGREGOR M, DAVENPORT HT, JEGHER W, SEKELJ P, GIBBONS JE, DEMERS PP. The cardiovascular effects of halothane

- in normal children. *British Journal of Anaesthesia* 1958; **30**: 398-408.
2. BERRY FA. Inhalation agents in paediatric anaesthesia. *Clinics in Anaesthesiology* 1985; **3**: 515-37.
 3. COTE CJ. Pharmacology of anesthetic agents, narcotics and sedatives. In: RYAN JF, COTE CJ, TODRES LD, GOUDSOUZIAN NG, eds. *A practice of anesthesia for infants and children*. London: Grune & Stratton, 1986: 77-95.
 4. GREGORY GA, EGER EI II, MUNSON ES. The relationship between age and halothane requirements in man. *Anesthesiology* 1969; **30**: 488-91.
 5. FRIESEN RH, LICHTOR JL. Cardiovascular depression during halothane anesthesia in infants: a study of three induction techniques. *Anesthesia and Analgesia* 1982; **61**: 42-5.
 6. BARASH PG, GLANZ S, KATZ JD, TAUNT K, TALNER NS. Ventricular function in children during halothane anesthesia: an echocardiographic evaluation. *Anesthesiology* 1978; **49**: 79-85.
 7. WOLF WJ, NEAL MB, PETERSON MD. The hemodynamic and cardiovascular effects of isoflurane and halothane anesthesia in children. *Anesthesiology* 1986; **64**: 328-33.
 8. NEAL MB, PETERSON MD, GLOYNA D, CASTA A, ARENS JF, WOLF WJ. Hemodynamic and cardiovascular effects of halothane and isoflurane anesthesia in children. *Anesthesiology* 1984; **61**: A437.
 9. FRIESEN RH, LICHTOR JL. Cardiovascular effects of inhalation induction with isoflurane in infants. *Anesthesia and Analgesia* 1983; **62**: 411-4.
 10. COTE CJ, GOUDSOUZIAN NG, LIU LMP, DEDRICK DF, ROSOW CE. The dose response of intravenous thiopental for the induction of general anesthesia in unpremedicated children. *Anesthesiology* 1981; **55**: 703-5.
 11. BECKER KF, TONNESON AS. Cardiovascular effects of plasma levels of thiopental necessary for anesthesia. *Anesthesiology* 1978; **49**: 197-200.
 12. SELTZER JL, GERSON JI, ALLEN FB. Comparison of the cardiovascular effects of bolus v. incremental administration of thiopentone. *British Journal of Anaesthesia* 1980; **52**: 527-9.
 13. PURCELL-JONES G, JAMES IG. The characteristics of propofol ('Diprivan') for induction of general anaesthesia for paediatric surgery. *Postgraduate Medical Journal* 1985; **61** (Suppl.): 115.
 14. REDFERN N, STAFFORD MA, HULL CJ. Incremental propofol for short procedures. *British Journal of Anaesthesia* 1985; **57**: 1178-82.
 15. MCCULLOCH MJ, LEES NW. Assessment and modification of pain on induction with propofol (Diprivan). *Anaesthesia* 1985; **40**: 1117-20.
 16. BROOKER J, HULL CJ, STAFFORD M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40**: 91-2.
 17. BROOKER J, REDFERN N. Pain on injection with propofol. *Anaesthesia* 1986; **41**: 1062.
 18. KAWAR P, DUNDEE JW. Frequency of pain on injection and venous sequelae following the I.V. administration of certain anaesthetics and sedatives. *British Journal of Anaesthesia* 1982; **54**: 935-8.
 19. GIBB D. Drug interactions in anaesthesia. *Clinics in Anaesthesiology* 1984; **2**: 485-512.
 20. GLEN JB. The animal pharmacology of ICI 35 868: a new I.V. anaesthetic agent. *British Journal of Anaesthesia* 1980; **52**: 230P.
 21. ROLLY G, VERSICHELEN L, HERREGODS L. Cumulative experience with propofol ('Diprivan') as an agent for the induction and maintenance of anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 96-100.

Cocaine absorption from the nasal mucosa

L. BROMLEY AND A. HAYWARD

Summary

The absorption of cocaine from the nasal mucosa was measured by serial plasma analysis in patients who received nasal cocaine for routine nasal surgery using the modified Moffett's method. Two groups were compared: one received cocaine alone and one with adrenaline 1:1000 added. Changes in pulse rate and blood pressure were recorded in each group. The group that received intranasal cocaine and adrenaline solution had significantly lower plasma cocaine levels. There was no significant difference in cardiovascular parameters between the two groups.

Key words

Anaesthetic techniques, regional; topical.

Anaesthetics, local; cocaine.

Cocaine was first used in modern local analgesia by Koller in 1884¹ and was first combined with adrenaline in 1930 by Braun.¹ Moffett² described a method of providing local anaesthesia to the nose in 1947. This was a solution composed of 2 ml cocaine hydrochloride 8%, 1 ml adrenaline 1:1000 and 2 ml sodium bicarbonate, 1%. This solution was administered originally to allow surgery on the nasal mucosa of awake patients.

It has become the practice latterly in some centres to administer a solution of cocaine and adrenaline of similar constitution as Moffett's to the nasal mucosa of anaesthetised patients.³ This is used to provide vasoconstriction in the mucosa and to improve the operative field. We dilute the solution up to 20 ml with sterile water at the Royal National Throat, Nose and Ear Hospital, London, to ensure contact with the entire nasal mucosa. The inclusion of adrenaline is intended further to increase vasoconstriction and to reduce the absorption of cocaine in order to limit its toxic effects.

The aim of this study was to quantify the absorption of cocaine in the presence and absence of adrenaline and to observe any changes in pulse rate and arterial blood pressure.

Methods

The study was carried out on 30 adults in the age range 18–50 years who underwent routine nasal surgery (submucosal resection). All patients were assessed pre-operatively as ASA grade 1 and informed consent was obtained. The anaesthetic technique was standardised: premedication with

papaveretum and hyoscine, induction with thiopentone up to 4 mg/kg and tracheal intubation after suxamethonium 1 mg/kg. The patients were allowed to breathe spontaneously a mixture of nitrous oxide and oxygen with halothane up to 2% through a Magill breathing system. Continuous monitoring of the electrocardiogram and arterial blood pressure using a Simonson and Weil diascope and Critikon Dinamap 845 was commenced at induction of anaesthesia.

The patients were randomly allocated into two equal groups matched for age and sex. All patients received a nasal instillation of 20 ml of solution. Group 1 received 2 ml cocaine hydrochloride 10%, 2 ml sodium bicarbonate 1% and 16 ml sterile water. Group 2 received 2 ml cocaine hydrochloride 10%, 2 ml sodium bicarbonate 1%, 1 ml adrenaline 1:1000 and 15 ml sterile water. The dilute solution was established to have the same pH as the concentrated solution, in order to ensure the same bio-availability of the cocaine in each.

The technique of instillation was standardised: a throat pack was inserted and the patient positioned with the neck extended by placing a pillow under the shoulders. Baseline readings of pulse rate and arterial blood pressure were recorded and then the appropriate solution instilled into the nose. Arterial pressure and pulse rate were then recorded at 3, 5, 10, 15 and 30 minutes. Venous blood samples from an indwelling cannula were taken at 10, 15, 30 and 60 minutes after instillation. For each sample, 10 ml of blood were transferred to a lithium heparin tube that contained additional sodium fluoride to prevent degradation of cocaine by plasma esterases. Plasma was immediately separated from the blood sample and stored frozen.

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Table 1. Mean plasma (SD) plasma cocaine concentrations, mg/litre.

	Time after instillation, minutes			
	10	15	30	60
Cocaine only group	0.99 (0.411)	0.95 (0.405)	0.82 (0.362)	0.49 (0.236)
Cocaine and adrenaline group	0.31 (0.68)	0.08 (0.054)	0.11 (0.065)	0.13 (0.077)

Table 2. Mean (SD) systolic blood pressure, mmHg.

	Time after instillation, minutes					
	0	3	5	10	15	30
Cocaine only group	111 (12.9)	107 (15.4)	115 (16.0)	118 (13.9)	118 (14.8)	117 (15.7)
Cocaine and adrenaline group	116 (18.3)	105 (14.0)	110 (17.0)	114 (17.9)	114 (14.1)	112 (18.2)

Table 3. Mean (SD) pulse rate, beats/minute.

	Time after installation, minutes					
	0	3	5	10	15	30
Cocaine only group	62 (14.3)	60 (17.1)	62 (15.1)	67 (18.0)	70 (17.7)	71 (19.2)
Cocaine and adrenaline group	62 (11.3)	54 (11.6)	62 (14.4)	63 (13.2)	63 (12.4)	64 (9.51)

The plasma was allowed to thaw prior to analysis and aliquots (500 μ l) were extracted at an alkaline pH into butyl acetate with pentazocine as an internal standard. Sample extracts were analysed by gas-liquid chromatography using a 3% caps OV-1 column with nitrogen/phosphorus detection. The method was linear over the standard range 0.2–2.0 mg/litre and the limit of detection of cocaine was 0.02 mg/litre.⁴

Statistical analysis was with the unpaired Student's *t*-test.

Results

The mean plasma cocaine levels for each group at each sampling time are shown in Table 1. The mean systolic arterial blood pressures and mean pulse rates are shown in Tables 2 and 3, respectively.

There was a highly significant difference between the plasma levels of cocaine in the two groups; the absorption of cocaine was reduced by the addition of adrenaline. This effect was most marked at the 15-minute sampling time, where there was a ten-fold difference in the means of the two groups ($p < 0.005$). There were no significant differences between arterial blood pressure and heart rate in the two groups.

Three patients in the cocaine plus adrenaline group developed bradycardia (pulse rates 42, 35, 42 beats/minute) 3 minutes after instillation of the solution. One was accompanied by a run of ventricular ectopics and required intravenous administration of atropine.

Discussion

Cocaine in ear, nose and throat surgery is used in the nose primarily for its vasoconstrictor action. Its local anaesthetic effect makes a secondary contribution to general anaesthesia. The effects of cocaine on the cardiovascular system are attributed to its ability to block the re-uptake of nor-adrenaline at sympathetic nerve terminals and thus to potentiate sympathetic activity.⁵ In this manner vasoconstriction is produced and the same mechanism is held to

account for the tachydysrhythmias and increase in arterial systolic blood pressure sometimes seen with moderate doses of cocaine. This potentiation of noradrenaline occurs both centrally and peripherally.

The reason for the incorporation of adrenaline into Moffett's solution is to intensify the vasoconstrictor effect and thus limit the absorption of cocaine into the systemic circulation. This carries a theoretical risk of increasing the circulating adrenaline,⁶ and this may lead to additional dysrhythmias in the presence of halothane anaesthesia.

Adriani and Campbell⁷ in a previous study showed no significant difference in the absorption of cocaine if adrenaline was added to the solution. However, this work was carried out on dogs and the assay of cocaine using a colorimetric method, is 50–100 times less sensitive than the gas-liquid chromatographic method used in our study.

Van Dyke *et al.*⁸ measured plasma cocaine after intranasal application prior to nasal intubation. They found no change in pulse rate or blood pressure and a peak absorption at 30–60 minutes. The peak absorption in our study occurred by 30 minutes; however, in the study of Van Dyke *et al.*⁸ no surgery was carried out on the nose, and the more rapid absorption in our patients may be due to the commencement of surgery. Cocaine is absorbed rapidly from the nasal mucosa; the euphoria derived from sniffing of cocaine in the conscious patient is reported to occur within 3–5 minutes.⁹ We found no significant difference between the two groups as regards pulse and blood pressure recordings, which agrees well with Van Dyke's previous study.⁸

Three patients in the cocaine and adrenaline group developed a significant bradycardia 3 minutes after instillation of the solution. Cocaine, when given systemically, is known to slow the heart via central vagal stimulation. This is usually associated with low plasma levels of cocaine; however, in two of these patients the highest levels of plasma cocaine also occurred, 10 minutes after instillation (2.25 and 1.68 mg/litre). Both these levels approach those associated with toxicity (3.0 mg/litre).¹⁰ There was no clinically obvious reason why these patients should absorb cocaine so rapidly.

A minority of conscious patients who receive cocaine paste for local anaesthesia, have a vasovagal-type reaction that consists of bradycardia and hypotension.¹¹ Some of these reactions may be accounted for by an idiosyncratic rapid absorption of cocaine, as occurred in our patients. These reactions are said not to be dose dependent, which further supports an idiosyncratic mechanism.

Chiu *et al.*¹² reported myocardial infarction that occurred in a patient who received 25% cocaine paste whilst awake. This patient had previously used cocaine recreationally and experienced chest pain. The cardiovascular disturbance included tachycardia but unfortunately no plasma cocaine levels were measured. It is therefore not possible to prove that this particular reaction was due to idiosyncratic rapid absorption, but it represents a reasonable hypothesis.

This study shows that the absorption of cocaine is significantly reduced by the inclusion of adrenaline 1:1000 in solution applied to the nasal mucosa. There are no significant changes in pulse rate and arterial blood pressure with the inclusion of adrenaline, even in the presence of 2% halothane. We are unable to account for the unusually high levels of cocaine recorded in two patients in the cocaine and adrenaline group, but suggest that an idiosyncratic rapid absorption may be responsible for these results and also for the so-called 'cocaine reaction' seen occasionally in awake patients.

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References

1. ATKINSON RS, RUSHMAN GB, ALFRED LJ. *A synopsis of anaesthesia*, 8th edn. Bristol: John Wright and Sons Ltd, 1977.
2. MOFFETT AJ. Nasal analgesia by postural instillation. *Anaesthesia* 1947; **2**: 31-4.
3. JOHNS ME, HENDERSON RL. Cocaine use by the otolaryngologist: a survey. *Transactions of the American Academy of Ophthalmology and Otolaryngology* 1977; **84**: 969-73.
4. ESSEX E. Personal communication.
5. MURDOCH RICHIE J, GREEN NM. Local anaesthetics. In: GOODMAN A, GILLMAN A, eds. *The pharmacological basis of therapeutics*, 6th edn. New York: Macmillan, 1980: 307-8.
6. BARASH PG, KOPRIVA CJ, LANGOU R, VAN DYKE C, JATLOW P, STAHL A, BYCK R. Is cocaine a sympathetic stimulant during general anesthesia? *Journal of the American Medical Association* 1980; **243**: 1437-9.
7. CAMPBELL D, ADRIANI J. Absorption of local anesthetics. *Journal of the American Medical Association* 1958; **168**: 873-7.
8. VAN DYKE C, BARASH PG, JATLOW P, BYCK R. Cocaine: plasma concentrations after intranasal application in man. *Science* 1976; **191**: 859-61.
9. FISCHMAN MW, SCHUSTER CR, RESNEKON L. Cardiovascular and subjective effects of intravenous cocaine administration in humans. *Archives of General Psychiatry* 1976; **33**: 983-9.
10. WETLY CV, WRIGHT RK. Death caused by recreational cocaine use. *Journal of the American Medical Association* 1979; **24**: 2519-22.
11. MAYER E. The toxic effects following the use of local anesthetics. *Journal of the American Medical Association* 1924; **82**: 876-85.
12. CHIU YC, BRECHT K, DASGUPTA DS, MHOOON E. Myocardial infarction with topical cocaine anesthesia for nasal surgery. *Archives of Otolaryngology—Head and Neck Surgery* 1986; **112**: 988-90.

Anaesthesia for valvuloplasty

A. CHAFFE, M. J. FAIRBRASS AND R. R. CHATRATH

Summary

Two years' experience of anaesthesia for percutaneous balloon valvuloplasty in children is presented and the problems associated with this procedure are discussed.

Key words

Anaesthesia; cardiac.

Surgery; cardiac, balloon valvuloplasty.

Percutaneous transluminal balloon valvuloplasty is used increasingly in paediatric cardiology to treat pulmonary valve stenosis and, more recently, aortic valve stenosis. We report a retrospective series of 20 cases performed under general anaesthesia in this unit.

Methods

Twenty patients aged from 1–19 years of age were admitted under the care of the paediatric cardiologists between January 1985 and December 1986. Fifteen had pulmonary valve stenosis and five, aortic valve stenosis. One of the patients with pulmonary valve stenosis had two valvuloplasties performed a few months apart.

All patients were premedicated with morphine 0.2 mg/kg intramuscularly one hour pre-operatively. Anaesthesia was induced with thiopentone 3 mg/kg followed by pancuronium 0.1 mg/kg to facilitate oral tracheal intubation. Intermittent positive pressure ventilation was carried out manually with a T-piece in patients who weighed less than 20 kg and with a Bain system in those more than 20 kg, with 33% oxygen in nitrous oxide supplemented with 0.5% halothane. An intravenous infusion of crystalloid was started. The ECG was monitored from arrival in the laboratory; arterial blood pressure was monitored initially with a cuff and later by a transducer attached to the cardiac catheter. Blood gases were taken for analysis from the catheter at various stages during the procedure.

The patients scheduled for pulmonary valvuloplasties first had right heart angiography via a catheter inserted in the femoral vein to demonstrate right ventricular size and function and to measure the pressure gradient across the pulmonary valve. The catheter was then changed, over a wire, to a balloon catheter and the balloon positioned across

the valve orifice. This was de-aired carefully and inflated by hand with a mixture of 50% contrast medium and 50% saline 0.9% until the waistline of the balloon caused by the stenotic valve disappeared. The inflation was held for 10–15 seconds. At least one minute was allowed to elapse before the next inflation to allow any bradycardia to settle and the inflation repeated as required for sufficient dilatation of the valve. The patients' lungs were ventilated with 100% oxygen for 2–3 minutes prior to, and during the time that the balloon was inflated. The balloon catheter was then removed and the angiogram repeated. Blood was taken from the catheter just prior to removal, to determine blood group, and for serum for any other tests required by the cardiologists. Firm pressure was applied to the puncture site after removal of the catheter, until the bleeding stopped.

The aortic valvuloplasties were performed in a similar manner but with left heart angiography and balloon dilatation via the femoral artery.

Residual muscular paralysis was reversed with neostigmine and atropine once the bleeding was under control, and the patients' tracheas extubated in the lateral position while a nurse maintained pressure on the puncture site. The intravenous infusion was maintained on return to the ward, until that evening and regular observations made of pulse, respiration and the puncture site.

Results

A satisfactory reduction in obstruction was obtained in 13 of the 15 patients who underwent pulmonary valvuloplasty, one was unchanged and two needed surgical relief of associated infundibular obstruction. Satisfactory results were obtained in three of the five patients who underwent aortic valvuloplasty and one needed surgical relief of sub-aortic

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Table 1. Results for pulmonary valvuloplasties.

Age (years)	Diagnosis	Complications
19	PS	None
1.5	PS	SVT on induction
3	PS,RVOTO	Bradycardia on balloon inflation requiring atropine; postoperative haematuria and pyrexia
11.5	PS,RVOTO	None
3.5	PS	None
4	PS	250 ml blood loss Second valvuloplasty performed with minor postoperative haemorrhage
3	PS	None
2	PS	None
3.5	PS	None
4	PS	None
1	PS	Two balloons used, both burst
13	PS	None
9	PS	None
1	PS	None
1	PS	None

PS, pulmonary stenosis; RVOTO, right ventricular outflow tract obstruction; SVT, supraventricular tachycardia.

Table 2. Results for aortic valvuloplasties.

Age (years)	Diagnosis	Complication
8	AS	Minor bruise in groin
3.5	AS	Moderate postoperative haemorrhage
11	AS	Postoperative haemorrhage 25–30 ml Unable to keep balloon in valve orifice
6	AS	Minor postoperative haemorrhage
16	AS and Turner's syndrome	None

AS, aortic stenosis.

obstruction. Valvuloplasty was impossible in one patient since the force of blood ejected from the left ventricle prevented the balloon remaining in the valve orifice.

Two of the patients who had pulmonary valvuloplasties developed dysrhythmias that required treatment. An 18-month-old child with pulmonary stenosis developed supraventricular tachycardia on induction of anaesthesia, and this required cardioversion to revert to a normal rate. A 3-year-old developed bradycardia on balloon inflation, which did not settle on deflation of the balloon but needed atropine to restore a more rapid rate. Two balloons were needed for adequate dilatation in one case and both balloons burst on final inflation.

The commonest problem encountered was bleeding. All patients had intravenous infusions during the procedure since minor blood loss occurred around the catheter at the puncture site, and blood samples were taken during angiography. One 4-year-old patient required a 250-ml transfusion during the procedure. Four patients had minor postoperative haemorrhage, one of 25–30 ml, the others of smaller amounts. All these settled with firm pressure applied to the wound.

The average duration of this operation was 40 minutes. The patient was draped with both plastic and green sheets to prevent hypothermia while on the table; the laboratory was also heated to 80°C before use, monitored and kept at this temperature throughout.

One patient developed a postoperative pyrexia and minor

haematuria but these both settled spontaneously. However, he was kept in hospital for observation for 3 days rather than the routine 24 hours.

Discussion

The technique of percutaneous balloon valvuloplasty for congenital pulmonary stenosis is still relatively new but the results are so encouraging^{1,2} that it is rapidly becoming the treatment of choice for this condition. The procedure in aortic stenosis is even more recent; longer-term follow up results are not available but it is thought that this is a palliative procedure and surgical valvotomy or replacement may be necessary at a later date.¹ However, it may be used to delay surgery until the child is older and therefore more able to withstand open heart surgery. It may be used as the definitive procedure in those who are unfit for surgery,^{1,3} such as elderly patients with calcific aortic stenosis.

Anaesthesia for balloon valvuloplasty, as for cardiac catheterisation, should minimise any alteration to the cardiovascular system. The majority of the procedures in adults may be carried out with the patient awake or with light sedation. Heavier sedation should be avoided since it may cause respiratory depression which leads to the cardiovascular changes associated with carbon dioxide retention.⁴ General anaesthesia avoids an unpleasant and frightening experience for children and ensures the immobility that is needed for accurate imaging with digital subtraction techniques.

The use of a narcotic premedication, morphine 0.2 mg/kg, causes little cardiovascular change and ensures that the majority of patients are calm before induction of anaesthesia. Children usually sleep for a few hours once they return to the ward and that stops untoward movement that might restart haemorrhage from the puncture site in the groin. Vomiting was thought to have initiated postoperative bleeding in two or three cases, although not recorded in the notes. This may have been associated with the morphine, and future vomiting may be reduced by concomitant use of an antiemetic.

The technique of induction and maintenance of anaesthesia should cause as little disturbance to the cardiovascular system as possible. Intermittent positive pressure ventilation with 33% oxygen in nitrous oxide with 0.5% halothane as a supplement was found to cause very little change in the measured variables during these cases and provided satisfactory conditions for the cardiologists. Halothane was never required in concentration greater than 0.5% and was avoided in the rare cases of repeat procedures, where iso-flurane was used instead. Pancuronium was chosen as the relaxant since the tachycardia it produces offsets the later bradycardias, maintains cardiac output and its duration of action is such that one dose is sufficient for the entire procedure. We consider that it would be necessary to give atropine in addition to pre-empt later problems had a newer relaxant been chosen, and this would produce a tachycardia with a possible longer duration than the pancuronium.

Induction was carried out with particular care in patients with aortic stenosis and a fixed cardiac output, because there is a tendency for the blood pressure to decrease if the thiopentone is given rapidly. A combination of ketamine and fentanyl was used for aortic valvuloplasty with satisfactory results⁵ and we may use ketamine in our future management of these cases.

Hand ventilation gave good control of the apnoeic phases needed during filming, and carbon dioxide levels were monitored with blood gas samples during the procedure. Ideally, an end tidal carbon dioxide monitor would be used with a pulse oximeter but constraints on both finances and space in the laboratory prevent this. We now have a Sheffield Infant ventilator which we intend to evaluate for use during cardiological cases.

It was felt that the risks of arterial cannulation outweighed the benefits since pressure was measured via the catheter except for the brief period prior to catheterisation where a cuff was used, and arterial blood gases were also taken from the catheter during the procedure.

All the problems associated with cardiac catheterisation may occur during these cases.⁶ Those due to the use of contrast medium include allergy, anaphylaxis and cardiac dysrhythmias (manufacturer's data sheet). Iopamidol (Niopam, Merck) was the agent used and neither of the dysrhythmias which occurred was in association with its injection.

The volume of contrast medium used, the heparinised flush used to keep the catheters patent and the hyperosmolarity of the contrast medium, may all contribute to hypervolaemia in small children. Loss of blood both during the procedure around the catheter and afterwards, presented the commonest problem. The aortic valvuloplasties, as expected, presented with the highest proportion of post-operative bleeding (four of five cases) since the puncture site was arterial. The regional blood transfusion centre at Killingbeck is within a mile of the hospital and blood can be available within 30 minutes if required urgently. We consider it would be prudent to have blood on hand prior to aortic valvuloplasties in situations where blood is not rapidly available and to 'group and save' prior to pulmonary valvuloplasties.

Care was taken to avoid the possibility of a gas embolism during the angiography injection of contrast medium with the automatic injector (Angiomat 3000). The balloon used to dilate the valve orifice was also flushed through several times with a mixture of 50% contrast medium in 0.9% saline before insertion. This was to prevent gas embolism should the balloon burst, as happened twice in this series.

Dysrhythmias are not uncommon during this procedure. Ectopic beats due to mechanical irritation may occur as the catheter passes through the heart. Similarly, bradycardias due to reduced myocardial perfusion may occur while the balloon is inflated. Diminished blood flow through the pulmonary bed to the left heart occurs when the pulmonary valve is occluded and myocardial perfusion, though present, is reduced. However, there is no flow at all through the coronary arteries when the aortic valve is occluded. This, together with the increase in intraventricular pressure that causes subendocardial compression, plays a great part in the genesis of these bradycardias.⁵ Normally, these settle spontaneously once the balloon is deflated. One case in our series, however, and three cases in another study² required atropine. The patients' lungs were ventilated with 100% oxygen prior to balloon insufflation in all our cases, to ensure optimal oxygenation of the myocardium prior to the reduction of perfusion. The increase in left ventricular pressure when the aortic valve was occluded made it difficult, and in one case impossible, to keep the inflated

balloon in the aortic valve. A case was reported where simultaneous caval balloon inflow occlusion reduced this increase in pressure and thus avoided this complication.⁵

Additional problems are associated with anaesthesia in the X ray department and cardiology laboratory. Anaesthetics given outside the operating theatre must all be to the same standard as those given inside the theatre and the full range of drugs, equipment and monitoring devices should be available, together with a trained assistant. There must be adequate light to monitor the patient's colour and the anaesthetic machine controls. The ECG and pressure trace from the catheter are displayed on overhead monitors in the Killingbeck laboratory and are therefore clearly visible at all times. All the tubing and intravenous lines must be secure and long enough to allow movement of the screening apparatus and table.

Only one case in our series needed surgical relief of a subvalvular obstruction. It was considered that in this case a period of time in intensive care for ventilation and stabilisation of the cardiovascular parameters, with surgery on the next available list, was preferable to emergency surgery with its attendant hazards. Therefore, no emergency theatre is kept available whilst these procedures are performed.

Percutaneous balloon dilatation is used increasingly by cardiologists for the dilatation not only of stenotic valves but also of coarctation of the aorta and of postoperative restenosis, and of postoperative stenoses that occur after correction of tetralogy of Fallot, Blalock-Taussig shunts and Mustard procedures. The same anaesthetic technique has been used in this hospital for these cases and for related procedures in both neonates and children with success. The use of these techniques by cardiologists will probably demand a greater number of anaesthetics to be performed in the cardiology department, with all the implications that this carries of an increased commitment of anaesthetic time. These procedures are not without significant potential hazards and therefore carry a degree of risk to the patient, although this is probably less than that associated with surgery. Awareness of the potential problems and anticipation of the complications are mandatory if safe anaesthesia is to be given in these cases.

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References

1. WREN C. Balloon valvuloplasty and angioplasty in cardiology. *Hospital Update* 1986; **12**: 935-45.
2. KAN JS, WHITE RI, MITCHELL SE, ANDERSON JH, GARDNER TJ. Percutaneous transluminal balloon valvuloplasty for pulmonary valve stenosis. *Circulation* 1984; **69**: 544-60.
3. SANDERSON JE, CAVANAGH PH, FALMER RBG. Inoperable aortic stenosis in the elderly: benefit from percutaneous transluminal valvuloplasty. *British Medical Journal* 1987; **294**: 510.
4. SMITH G, AITKENHEAD AR. *Textbook of anaesthesia*. Edinburgh: Churchill Livingstone, 1985: 58.
5. KIEL EA, VAN DEVANTER SH, READINGER RI, DUNGAN WT, NORTON JB. Aortic balloon valvuloplasty with transluminal venous balloon inflow occlusion. *Pediatric Cardiology* 1986; **7**: 103-5.
6. JORDAN SC, SCOTT O. *Heart disease in paediatrics*, 2nd edn. London: Butterworths, 1981: 44-7.

The effects of injected solution temperature on intravenous regional anaesthesia

D. L. PAUL, M. R. LOGAN AND J. A. W. WILDSMITH

Summary

Ten healthy volunteers received three standard Bier's blocks. Prilocaine 0.5%, 40 ml was injected at a solution temperature of 0°C, 22°C or 37°C. Recordings were made of sensory block, motor block, intravenous pressure, limb temperature and pain on injection. There were no differences between the three treatments in the rate of development or in the quality of block but there was a significant difference in the comfort of injection. Cold solutions caused most, and warm solutions least discomfort.

Key words

Anaesthetic techniques; intravenous, regional.
Anaesthetics, local; prilocaine.

Nerve conduction may be blocked by a number of agents but the only methods which have been used clinically with any reliability are cold and local anaesthetic drugs. Both have long been known to slow, and then block, conduction in experimental nerve preparations^{1,2} and it was suggested more recently that cold potentiates the *in vitro* action of local anaesthetic drugs.³ This led us to consider whether the temperature at which a local anaesthetic solution is injected might influence the development of the block. A study was devised to test this in subjects who received a standard, reproducible regional anaesthetic technique that employed a large volume of solution.

Methods

Ten healthy male volunteers gave informed consent to the study which was approved by the local ethical committee. Each subject received three Bier's blocks by a standard technique at intervals of at least 4 days. An orthopaedic tourniquet was applied over padding on the nondominant upper arm. Two Teflon cannulae were inserted in the same arm, one in a vein in the antecubital fossa and the other into a vein on the ulnar aspect of the dorsum of the hand. The same veins were used on each occasion. The arm was exsanguinated by elevation and compression of the brachial artery for one minute. The tourniquet was inflated to 250 mmHg and 40 ml prilocaine 0.5% injected over 120 seconds. The tourniquet was released 22 minutes after the start of the injection. The solution was at a different temperature on each occasion. This was standardised by

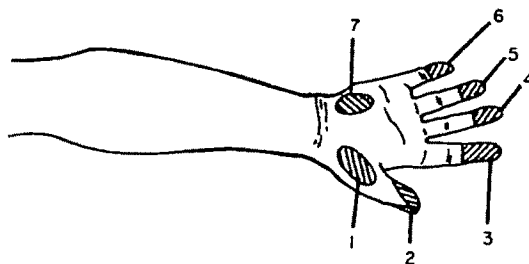


Fig. 1. Sites tested for sensation.

keeping the charged syringes for at least one hour either in a water bath that contained an ice–water mixture (0°C), or in water at room temperature (22°C) or water heated to 37°C as appropriate. The order of use of each solution temperature was randomised and unknown to the observer.

Sensation was tested at 2-minute intervals, at each of seven sites (Fig. 1) with a 27-gauge short bevel needle. Sensation was graded as sharp, blunt or absent. Motor power was assessed by asking the volunteer to squeeze maximally a bag of saline, the volume of which was adjusted to fit the hand comfortably. The pressure in the bag was measured with a calibrated transducer (Haslett), a twin-channel monitor (Roche Kontron) and an ultraviolet recorder (Bell and Howell). The monitor's other channel was used to record the venous pressure at the cannula placed in the antecubital fossa. The tourniquet was released 20 minutes after the end of the injection and recordings continued until the needle-prick felt sharp at every site and motor power had recovered to at least 80% of control.

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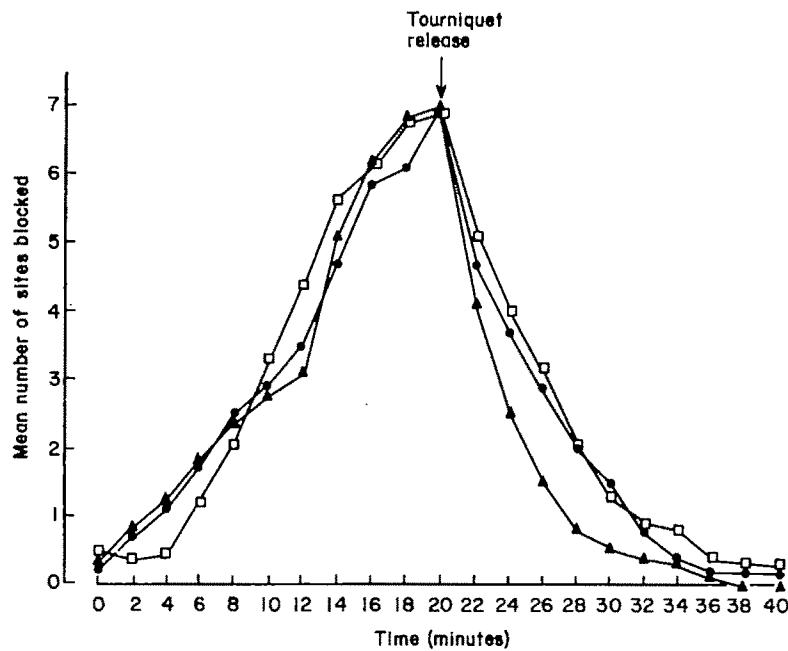


Fig. 2. Mean number of sites totally blocked, against time. \blacktriangle , 37°C; \square , 22°C; \bullet , 0°C.

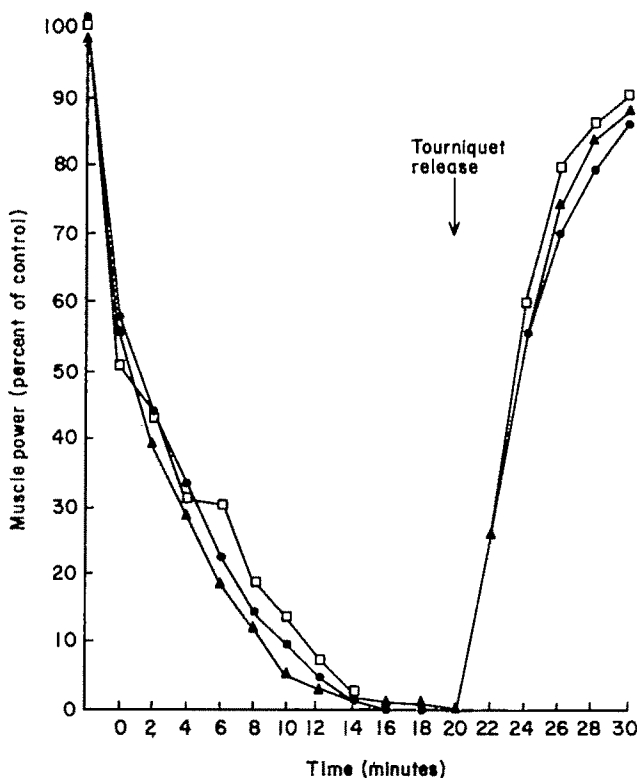


Fig. 3. Mean percentage of original muscle power, against time. \blacktriangle , 37°C; \square , 22°C; \bullet , 0°C.

The subject completed a visual analogue scale approximately 30 minutes after each injection, to grade the discomfort noted during injection.

Results

Complete sensory block was obtained at every site in each subject within 20 minutes of injection, no matter what the temperature of the solution. The rates of development of

Table 1. Mean (SD) values for maximum venous pressure and linear analogue score for each solution.

	0°C	22°C	37°C
Maximum venous pressure, mmHg	70 (15)	77 (32)	79 (43)
Linear analogue score	4.5 (3.4)	2.3 (1.9)	1.3 (2.3)

sensory block (indicated by mean number of sites blocked with time, Fig. 2) and motor block (indicated by mean percentages of original power with time, Fig. 3) were unrelated to solution temperature. All subjects 20 minutes after injection had lost at least 95% of measurable muscle power. The rates of return of sensory and motor function after tourniquet release were also the same irrespective of solution temperature. Maximum venous pressure occurred towards the end of the injection in most subjects but in none did it exceed 75% of tourniquet pressure (Table 1). Discomfort during injection was significantly different between the three groups ($p < 0.02$, Friedman test); the warm solution was the least, and the cold solution the most uncomfortable. Four subjects found the cold solution to be extremely unpleasant.

Discussion

Intravenous regional anaesthesia was chosen for this investigation because it is a simple technique in which a large volume of solution is injected into a limb isolated from the warming effects of the circulation. However, the volume of solution injected was small compared to that of the arm. The maximum calculated change in temperature would not be more than 1°C if it is assumed that the solution and arm have similar specific heat capacities. Measurements of skin temperature made during injection indicated figures as low as 11°C but these returned to control readings shortly after completion of the injection. No assumptions about arm core temperature can be made from surface readings

but it seems unlikely that any significant change occurred. It is also unlikely that the use of ice-cold solutions for other local anaesthetic procedures would have any significant cooling action.

It was anticipated that vasoconstriction would be produced by the cold solution and this might cause a greater intraluminal pressure, with an increased risk of leak of local anaesthetic solution past the tourniquet, so venous pressure was measured at the cubital fossa. Solution temperature had no effect on venous pressure at the cubital fossa during intravenous regional anaesthesia at the rate of injection used.

The only significant difference between the groups was in the discomfort experienced on injection. Pain during injection of the cold solution was very marked: one volunteer found it to be almost unbearable and three others found it extremely unpleasant. Ice-cold saline was injected into the isolated forearm of two subjects during a pilot study and neither was able to tolerate the rate of injection used in the formal study. The use of a local anaesthetic drug seems to be necessary to overcome the adverse effects of cold. The pain could be caused by distension of vessels constricted by cold or by direct cold injury. We decided, because of the latter possibility, that it would be inadvisable to proceed with our original plan and inject cold solutions into con-

finer spaces such as the brachial plexus or epidural space.

In contrast, the 37°C solution caused no distress to nine of the subjects. Seven subjects noted that the warm solution caused no pain at all, and three indicated that the sensation during injection was almost pleasant! This agrees with observations made by ophthalmologists⁴ and dentists (M.R.S. Malone, personal communication) that prewarmed local anaesthetic solutions cause less discomfort to patients. It seems that warming of local anaesthetic solutions prior to injection is of practical benefit but that cooling them is not.

References

1. GASSER HS, ERLANGER J. The role of fibre size in the establishment of a nerve block by pressure or cocaine. *American Journal of Physiology* 1929; **88**: 581-91.
2. FRANZ DN, IGGO A. Conduction failure in myelinated and non-myelinated axons at low temperatures. *Journal of Physiology* 1968; **199**: 319-45.
3. BOKESCH P, STRICHARTZ GR. Temperature modulation of local anesthetic block in mammalian nerve. *Regional Anesthesia* 1984; **9**: 46-7.
4. BLOOM LH, SCHEIE HG, YANOFF M. The warming of local anesthetic agents to decrease discomfort. *Ophthalmic Surgery* 1984; **15**: 603.

Which intravenous induction agent for day surgery?

A comparison of propofol, thiopentone, methohexitone and etomidate

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Summary

Eighty day patients for the vaginal termination of pregnancy were randomly allocated to receive thiopentone, propofol, methohexitone or etomidate as intravenous induction agents. The same anaesthetist administered the anaesthesia and all the observers were blind to the agents used. The results show that thiopentone and propofol produced the least sequelae at induction and in recovery. Furthermore, both agents produced a high quality of induction and recovery. All patients were discharged home 2 hours postoperatively and there was no obvious delay in recovery. This study has altered clinical practice in our Day Surgery Unit.

Key words

Anaesthesia; outpatient.

Anaesthetics, intravenous; thiopentone, methohexitone, etomidate, propofol.

Propofol has been extensively investigated in day case anaesthesia.¹ Any anaesthetic induction agent for day surgery should ensure a smooth induction, good immediate recovery with minimal postoperative sequelae and a rapid return to street fitness.²

Thiopentone is still deservedly popular for inpatient procedures because of the smooth induction offered and many anaesthetists continue to use this agent for day cases in spite of the drug's known slow metabolism.³ Methohexitone has been preferred in Cambridge for many years for short operative procedures, although it is less than ideal and produces pain on injection, involuntary movements, hiccoughing and coughing on induction.⁴

Etomidate is rapidly metabolised with minimal cardiovascular effects but the involuntary movements encountered present problems.⁵ Propofol was introduced recently and offers swift induction⁶ and rapid recovery,⁷ but it is more expensive than thiopentone. Furthermore, it may produce pain on injection, apnoea and occasional bradycardia with hypotension.⁶

Most studies to date which have compared the effectiveness of propofol against the standard anaesthetic induction agents have not been blind. We have experience of 2000 propofol administrations in a purpose-built day surgical unit so it was decided to compare critically thiopentone, propofol, methohexitone and etomidate. The main aims of the study were to assess the induction characteristics, postoperative sequelae and recovery afforded by these four induction agents.

Methods

Local ethical committee approval was granted for the study. Eighty day patients aged 16–45 years scheduled for vaginal termination of pregnancy were randomly allocated to one of four treatment groups. A similar group of 20 patients acted as a group for comparison for the visual perception test, three tests being performed in the pre-operative period.

All patients gave informed consent on admission to the day unit. A pre-operative patient medical assessment questionnaire⁸ was completed and those with a history of drug allergy, serious medical disease or obesity were not studied.

All anaesthetics were administered by one anaesthetist (T.W.O.) who was aware of the induction agent administered but who took no part in the assessments. None of the other investigators knew which drug was given. No premedication was prescribed and patients were given alfentanil 7 µg/kg intravenously via a 23-gauge needle inserted in the dorsum of the nondominant hand. The anaesthetic induction agents, which were given randomly, were either thiopentone 2.5% 5 mg/kg, propofol 1% 2.5 mg/kg, methohexitone 1% 1.5 mg/kg or etomidate 0.2% 0.3 mg/kg with supplements of the same agent as required. One ml of 1% plain lignocaine solution was added to the propofol and methohexitone, the standard practice in our day unit. It has not been our practice to add lignocaine to either thiopentone or etomidate and hence it was omitted

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Table 1. Mean (SD) age, weight, duration of anaesthesia and alfentanil dosage in the series.

	Thiopentone (n = 20)	Propofol (n = 20)	Methohexitone (n = 20)	Etomidate (n = 20)	p
Age, years	23.1 (6.3)	25.1 (6.3)	23.8 (6.3)	25.2 (6.5)	NS
Weight, kg	61.3 (10.1)	57.9 (9.2)	61.3 (7.8)	59.9 (9.4)	NS
Duration of anaesthesia, minutes	6.8 (1.5)	6.6 (1.4)	7.1 (1.5)	7.3 (0.9)	NS
Alfentanil, µg	427.5 (47.2)	420.0 (59.4)	445.0 (48.4)	427.5 (47.2)	NS

NS, Not significant.

Table 2. Number of side effects in each of the treatment groups.

	Thiopentone (n = 20)	Propofol (n = 20)	Methohexitone (n = 20)	Etomidate (n = 20)	p
Induction	3	14	27	42	< 0.001
During anaesthesia	2	7	18	14	0.01
Recovery					
Immediate	12	10	16	32	0.001
At 1 hour	6	6	4	15	0.025
At 2 hours	3	0	1	2	0.35
Total	26	37	66	105	< 0.001

from these agents in this study. Patients were allowed to breathe spontaneously a mixture of 70% nitrous oxide in oxygen via a Bain system. Oxytocic drugs were not administered routinely.

Arterial blood pressure and heart rate were recorded prior to surgery, 2 minutes following induction using a Dinamap and then in the immediate recovery area. The anaesthetic induction time was recorded from the start of injection to loss of the eyelash reflex. Sequelae during anaesthetic induction were noted and the induction graded as excellent (4), good (3), fair (2) or poor (1). Steward's scoring test⁹ was used to assess immediate recovery and delayed recovery was recorded by Salt's visual perception test.¹⁰

The p values reported in the next section and in Tables 1–5 are the probability that the observed spread of results between the four groups occurred by chance. They are from tests of hypothesis and equality between the four groups: small p values (< 0.05) indicate genuine differences between the groups. The p values were calculated from variance-ratio *F* statistics on 3 and 76 degrees of freedom in Tables 1, 4 and 5, and from Pearson Chi-square statistics on 3 degrees of freedom in Tables 2 and 3.

Results

Table 1 shows that there was no significant difference between the groups with respect to age, weight, duration of anaesthesia and the dose of alfentanil administered.

Table 2 records the total number of side effects in the series. Methohexitone and etomidate both yielded high total side effect scores ($p < 0.001$).

Table 3 shows the side effects for each group at induction, in the recovery room and the main ward. A significantly higher incidence of spontaneous movement on induction ($p = 0.02$), muscle twitch ($p = 0.01$), tremor ($p < 0.001$) and injection site pain ($p = 0.002$) were noted with etomidate. This agent also yielded a higher incidence of restlessness in the recovery room ($p = 0.02$).

Table 4 records the mean (SD) scores for quality of induction and recovery in the series. Thiopentone and propofol were assessed to be the better induction agents ($p < 0.001$), whereas propofol produced the best recovery of the four drugs ($p = 0.002$). The immediate recovery

times for the propofol and methohexitone groups were significantly shorter ($p = 0.01$).

Table 5 shows the visual perception test scores for the series, as a measure of delayed recovery. The postoperative test at one hour was higher following thiopentone administration but there was no significant difference between the groups at one or at two hours after general anaesthesia. There was no significant difference in the visual perception test scores recorded by the group for comparisons on each of the three occasions tested (paired *t*-test). However, the large standard errors admit the possibility of clinically (albeit not statistically) significant differences between the groups. More patients, or improvements in the measurements of visual perception would be required to shed more light on this.

Discussion

It is of some importance with the recent expansion of British day surgery to select an anaesthetic induction agent with few side effects. The results presented in this series clearly indicate that both thiopentone and propofol produce significantly fewer sequelae at induction, during anaesthesia and in recovery than methohexitone and etomidate.

The objective assessment of the quality of induction showed thiopentone and propofol to be significantly better than either of the other two agents. Furthermore, the quality of recovery was significantly inferior in the etomidate group, while the highest score was in the propofol group. Immediate recovery was significantly more rapid in the propofol and methohexitone groups. However, this study failed to show any difference between the groups with respect to delayed recovery time as measured by a visual perception test. The patients left the recovery area more rapidly after propofol or methohexitone but there was no significant difference between the four agents studied by the time of discharge from the day unit. The results do not preclude the possibility of clinically significant differences between the groups and it would have been interesting to test all the patients 24 hours after anaesthesia.

Closer inspection of the sequelae observed at induction and recovery shows that etomidate produced the following side effects; spontaneous movement (30%), muscle twitch

Table 3. Selected side effects recorded in the series (only important or frequent side effects listed).

	Thiopentone (n = 20)	Propofol (n = 20)	Methohexitone (n = 20)	Etomidate (n = 20)	p
Induction					
Spontaneous movement	0	2	1	6	0.02
Twitch	0	2	5	8	0.01
Tremor	0	1	1	10	<0.001
Hiccough	0	1	6	3	0.02
Apnoea	3	6	8	4	0.28
Pain at injection site	0	2	4	9	0.002
First stage of recovery					
Restlessness	2	1	1	7	0.02
Nausea	1	1	3	4	0.34
Vomiting	2	0	2	4	0.22
In ward within 2 hours of anaesthesia					
Nausea	2	1	0	4	0.14
Vomiting	1	2	0	1	0.55

Table 4. Mean (SD) scores for quality of induction and recovery and immediate recovery times in the series.

	Thiopentone (n = 20)	Propofol (n = 20)	Methohexitone (n = 20)	Etomidate (n = 20)	p
Quality of induction	3.9 (0.3)	3.7 (0.5)	3.0 (1.0)	2.3 (1.1)	<0.001
Quality of recovery	3.1 (0.4)	3.3 (0.5)	3.1 (0.4)	2.7 (0.7)	0.002
Immediate recovery time, minutes	11.5 (4.5)	8.0 (2.3)	7.2 (2.9)	10.9 (6.4)	0.01

Table 5. Mean (SD) scores of visual perception test as measure of delayed recovery.

	Thiopentone (n = 20)	Propofol (n = 20)	Methohexitone (n = 20)	Etomidate (n = 20)	p
Pre-anaesthetic	153.2 (90.9)	144.2 (59.4)	142.0 (55.3)	133.3 (41.6)	0.81
1 hour postoperative	208.8 (83.4)	170.0 (53.5)	161.0 (61.6)	166.9 (66.9)	0.11
2 hour postoperative	133.3 (53.8)	130.5 (44.7)	128.8 (44.0)	132.8 (51.6)	0.99
1 hour - pre-operative	55.5 (78.6)	25.7 (56.1)	19.0 (70.0)	35.5 (66.6)	0.36
2 hour - pre-operative	-20.0 (61.3)	-13.8 (53.0)	-13.3 (38.5)	-0.5 (47.5)	0.67

(40%), tremor (50%), pain on injection (45%) and post-operative restlessness (35%). Both propofol and methohexitone yielded a high incidence of apnoea but this is a side effect with which anaesthetists should be able to deal. Finally, injection site pain, perhaps the most important side effect, was significantly more common after etomidate (45%) and methohexitone (20%). The addition of lignocaine to etomidate may reduce the incidence of pain on injection but is unlikely to reduce the incidence or severity of the other adverse effects observed. The incidence of injection-site pain is an acceptable 10% when 1 ml 1% lignocaine is added to 20 ml propofol. This incidence may be further reduced by injection of propofol into an antecubital fossa vein.¹¹

This study indicates that the choice of intravenous anaesthetic induction agent for day surgery lies between thiopentone and propofol. The former produces the lowest incidence of side effects on induction and the highest quality of induction, with an acceptable quality of recovery. Propofol produces more sequelae on induction but provides a high quality of recovery and a more rapid immediate recovery. Many anaesthetists may continue to use thiopentone in preference to propofol on the basis of lower cost. However, the saving is minimal when the overall cost-effectiveness of day case surgery is taken into account. The major saving is the reduction of inpatient beds and not the cost of an anaesthetic induction agent.

In conclusion, this study has altered our clinical practice. The use of methohexitone and etomidate has been dis-

continued. Propofol is now considered to be the induction agent of choice for day surgery. This agent compares favourably with thiopentone as concerns the incidence of induction sequelae but produces a swifter recovery.

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References

1. STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol 'Diprivan'. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3); 152-6.
2. OGG TW. Use of anaesthesia. Implications of day case surgery and anaesthesia. *British Medical Journal* 1980; **281**: 212-4.
3. MORGAN DJ, BLACKMAN GL, PAULL JD, WOLF LJ. Pharmacokinetics and plasma binding of thiopental. 1: Studies in surgical patients. *Anaesthesiology* 1981; **54**: 468-73.
4. ATKINSON RS, RUSHMAN GB, LEE JA. Methohexitone. In: ATKINSON RS, RUSHMAN GB, LEE JA, eds. *A Synopsis of anaesthesia*, 10th edn. Bristol: Wright, 1987: 236-7.
5. HOLDCROFT A, MORGAN M, WHITMAN JG, LUMLEY J. Effects of dose and premedication on induction complications with etomidate. *British Journal of Anaesthesia* 1976; **48**: 199-204.
6. CUMMINGS GC, DIXON J, KAY NH, WINDSOR JPW, MAJOR E, MORGAN M, SEAR JW, SPENCE AA, STEPHENSON DK. Dose requirements of ICI 35,868 (Propofol, 'Diprivan') in a new formulation for induction of anaesthesia. *Anaesthesia* 1984; **39**: 1168-71.

7. KAY B, HEALY TEJ. Propofol ('Diprivan') for outpatient cystoscopy. Efficacy and recovery compared with Althesin and methohexitone. *Postgraduate Medical Journal* 1985; **61** (Suppl 3): 108-14.
8. OGG TW. Assessment of pre-operative cases. *British Medical Journal* 1976; **1**: 82-3.
9. STEWARD DJ. A simplified scoring system for the post operative recovery room. *Canadian Anaesthetists' Society Journal* 1975; **22**: 111-13.
10. SALT PJ, FRANCIS RI, NOBLE J, OGG TW. Assessment of recovery from anaesthesia using a new visual perception test. *British Journal of Anaesthesia* 1985; **57**: 820P-1P.
11. MCCULLOCH MJ, LEES NW. Assessment and modification of pain on induction with propofol (Diprivan). *Anaesthesia* 1985; **40**: 1117-20.

Isoflurane for conscious sedation

M. R. C. RODRIGO AND J. B. ROSENQUIST

Summary

Isoflurane 0.5% in oxygen for conscious sedation was compared with placebo (oxygen) and with an equipotent concentration of nitrous oxide in oxygen, in patients scheduled for surgical removal of bilateral, similarly impacted lower third molars. The majority of patients were sedated with 0.5% isoflurane in oxygen and preferred it to both placebo and nitrous oxide in oxygen. It produced good operating conditions with cooperative patients and had no significant effect on vital signs. There were no significant intra- or postoperative adverse effects. Patients were street fit within 10 minutes after the end of the operation.

Key words

Anaesthetics, volatile; isoflurane.

Surgery; oral.

The technique of conscious sedation uses a drug or drugs to produce a state of depression of the central nervous system which enables treatment to be carried out but throughout which verbal contact with the patient is maintained. The drugs and techniques used should carry a margin of safety sufficiently wide to render unintended loss of consciousness unlikely.¹ Inhalational sedation in dentistry is such a method of conscious sedation and usually involves the use of nitrous oxide in oxygen. Nitrous oxide has several advantages in that it has a sweet odour,² is rapidly taken up and eliminated,³ does not produce cardiovascular⁴ or respiratory depression⁵ and, in addition, possesses analgesic properties.⁶

However, nitrous oxide has some drawbacks. It has been shown to interact with vitamin B₁₂ in the body, which is the co-enzyme for methionine synthesis, and thus to inhibit the formation of methionine and tetrahydrofolate. Lack of the former interferes with protein metabolism and myelination; lack of the latter interferes with DNA synthesis and produces megaloblastic changes and agranulocytosis.⁷ Abnormal values of dU suppression test of the bone marrow were reported in three out of 20 dentists who used nitrous oxide for sedation. Two dentists had hypersegmented polymorphs in their peripheral blood.⁸ In another report 15 patients who had inhaled subanaesthetic concentrations of nitrous oxide for long periods developed a condition that resembled subacute combined degeneration of the cord, which can also occur with vitamin B₁₂ deficiency.⁹ Another drawback is the alleged increased risk of

abortion in early pregnancy among those who work in an area polluted with nitrous oxide.^{10–12}

Methoxyflurane has also been tested for inhalational sedation.^{13,14} No major disadvantages were reported except that 0.35% methoxyflurane caused more patients to be uncooperative than did nitrous oxide.¹³ The possibility of nephrotoxicity^{15,16} and hepatotoxicity¹⁷ with repeated use of this agent has caused its further investigation for inhalational sedation to be abandoned.

Isoflurane is a volatile agent with rapid uptake and elimination,¹⁸ though to a lesser extent than nitrous oxide. It is minimally metabolised in the body¹⁹ and so the possibility of hepatic damage as with halothane¹⁷ or methoxyflurane,¹⁷ or of renal damage as with methoxyflurane^{15,16} or enflurane,²⁰ is remote. It has been shown neither to interfere with vitamin B₁₂ metabolism nor to be associated with an increased incidence of abortions among those who work in an atmosphere polluted with the agent. It has some analgesic properties: 0.7% provided adequate analgesia for vaginal delivery²¹ although the effectiveness may have been due to sedation rather than analgesia. Conscious sedation is used as an adjunct to local anaesthesia so analgesic properties of the sedative are not required.

The disadvantages of isoflurane are its ethereal odour,²² potency to induce sleep and, in high concentrations, respiratory and cardiovascular depression.^{23,24} However, in subanaesthetic concentrations it should produce conscious sedation with minimal depression and a tolerable odour. If so it would be an ideal agent for conscious

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sedation in dentistry. Thus it was considered worthwhile to investigate isoflurane for sedation during outpatient surgical procedures.

Methods

An inspired concentration of 0.5% of isoflurane in 100% oxygen was used because it is easy to administer and cardiorespiratory depression is minimal. The study was planned to be carried out in two parts. Firstly, in order to assess the suitability of 0.5% isoflurane in oxygen for conscious sedation, it was decided to compare this combination with a placebo (oxygen) and obtain the assessment of the surgeon and patients. Secondly, it was decided to compare 0.5% isoflurane in oxygen with an equipotent dose of nitrous oxide in oxygen. The minimum alveolar concentration of isoflurane in 100% oxygen is 1.15²⁵ and that of nitrous oxide in oxygen, 110.²⁶ An alveolar concentration of 0.5% isoflurane should thus be equipotent with 50% nitrous oxide in oxygen. However, the uptakes of the two gases differ: that of nitrous oxide is quicker by a factor of 1.5 at 10 minutes and the uptakes appear to remain parallel for at least 30 minutes (Fig. 1). An inspired

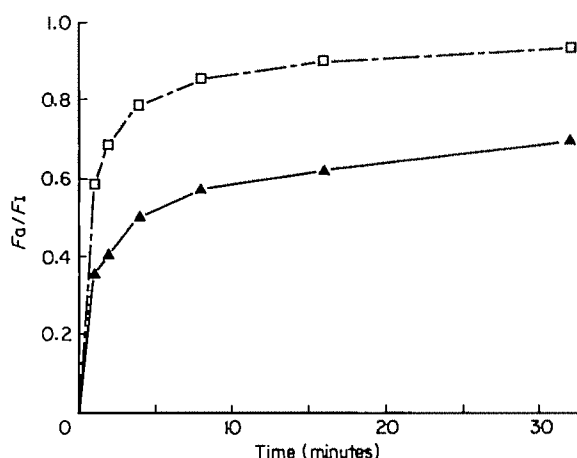


Fig. 1. Uptake of nitrous oxide³ (□) and isoflurane¹⁸ (▲).

concentration of 0.5% isoflurane in oxygen thus produces an alveolar concentration equipotent to an inspired concentration of 33% nitrous oxide in oxygen.

Surgical removal of bilateral, symmetrically impacted lower third molars permits the removal of one tooth in one session and the other tooth in a second. This model is unique in that two essentially identical outpatient operations carried out on healthy subjects offer the opportunity to study the intra-individual effect of drugs before, during and after surgery in a double-blind manner. Each patient acts as his own control in this model so variation that results from individual differences is eliminated. Moreover, fewer patients are required to demonstrate differences between treatments than in a parallel groups design. Lastly, the within-subject design permits evaluation of the patients' preference for the two methods.²⁷

It was therefore decided, using the above model, to determine the surgeons' and the patients' assessment of sedation with 0.5% isoflurane in oxygen, firstly in comparison with placebo and secondly in comparison with an equipotent dose of nitrous oxide in oxygen. The

investigation was approved by the Ethical Committee of the Faculty of Dentistry, University of Hong Kong.

Comparison with placebo

Thirteen nonpregnant patients of ASA grade 1 aged 18–40 years with no drug history or blockage of the nasal airway, referred for surgical removal of bilateral, similarly impacted lower third molars were included in the study after informed consent. Pre-operatively patients were asked to walk in a straight line, pivot around a point, perform a modified Romberg's test and ascend and descend a flight of stairs. Each patient completed two Trieger tests in the surgery after explanation. The time taken to perform each test was noted. The patient was then placed in a reclining position in a dental chair. Pulse rate and arterial blood pressure were recorded and respiration was observed immediately after the patient was positioned and throughout the procedure until recovery.

The anaesthetist placed a nasal mask on the nose and allowed the patient to adjust the mask so that it fitted comfortably. The nasal mask was connected to a Bain breathing system attached to a BOC Boyle's anaesthetic machine. Patients received at random, either 8 litres/minute oxygen or the same flow of 0.5% isoflurane in oxygen. Isoflurane was delivered from a recently calibrated Ohmeda Mk III Isotec vaporizer.* Expired gases were vented out of the surgery by an active scavenging system. The anaesthetic machine was covered as soon as it was ensured that the patient was receiving the correct mixture.

Five minutes were given for the agent to act and the patient was then shown two picture cards. The surgeon injected 2% lignocaine with adrenaline 1:80,000 and removed the impacted lower third molar on one side by a standard technique. Any erupted non-functional upper third molar on the same side was also extracted. The dose of lignocaine and the duration of surgery were recorded.

The surgeon, who did not know which gas mixture the patient received, assessed the operating conditions according to a standardised questionnaire. Patient co-operation during surgery was graded as: good, patient fully cooperative; fair, some interference or lack of response due to oversedation or undersedation; poor, operation difficult by virtue of oversedation or undersedation. The anaesthetist assessed the verbal response, recorded the arterial blood pressure and pulse rate and noted any adverse effects during sedation.

Oxygen 100% was given for 10 minutes at the end of surgery and the patients asked to complete a Trieger test. This was repeated every 10 minutes until the time taken was equal to or less than the pre-operative time. They were then asked to walk in a straight line, pivot around a point, perform a modified Romberg's test and ascend and descend a flight of stairs. Patients who could perform all these as well as they did pre-operatively, were considered to be fit for discharge.

Before discharge, patients were asked their opinion of relaxation during the surgical procedure, sleep, dreams, recollection of events during the surgical procedure, recollection of the cards shown at optimum sedation, pain and discomfort in the mouth and odour of the gas. At the time of discharge a postoperative questionnaire was

* Ohmeda, Elizabeth Way, Harlow CM19 5AB.

provided on adverse effects, to be answered and brought back on the postoperative visit for suture removal. Patients were provided with diflunisal for analgesia and the address and telephone number of the hospital to contact if a post-operative complication developed or advice was needed. They were instructed not to drive machinery for at least 2 hours.

The alternative sedation method was used at the second visit and surgical removal of the impacted third molar of the opposite side performed and the patient assessed as before. At the postoperative visit for suture removal after the second operation, the patient was asked following which sedation technique he was more relaxed, which sedation technique he preferred and why he preferred that sedation technique.

Comparison with nitrous oxide-oxygen

Twenty nonpregnant patients of ASA grade 1, aged 18–40 years with no drug history or nasal blockage, referred for surgical removal of bilateral similarly impacted lower third molars were included in the study after informed consent. The method was the same as above except that patients received at random, either 9 litres/minute 33% nitrous oxide in oxygen or the same flow of 0.5% isoflurane in oxygen in one operation and the alternative in the second. Patients received 9 instead of 8 litres/minute in this part of the study because it was easier to set the Rotameters to 33% nitrous oxide with the former total flow.

Ten minutes were given for the gases to act, since the uptakes of the gases parallel each other from 10 minutes (Fig. 1). Two picture cards were then shown. The surgeon assessed operating conditions as before and also graded the degree of sedation during the procedure as: light, moves but allows procedure to be done with verbal reassurance; moderate, responds to command, slight or no movement during procedure; deep, response to command sluggish.

After the second procedure the patient was asked, in addition to questions about relaxation and preference, whether he would like to undergo sedation with either agent in the future and, if not, which agent he disliked and why he disliked it.

Statistical comparisons were made using Fisher's exact probability and Chi-squared tests.

Results

Placebo

Thirteen patients were included in the study, five males and eight females. The age range was 19–32 years (mean 23, SD 3 years) and the weight range 44–71.5 kg (mean 55, SD 8 kg). The dose of local anaesthesia used was similar during both isoflurane and oxygen sedation and the duration of surgery was the same, 19 minutes (SD 6). The interval from the time of optimal sedation (5 minutes from the start of sedation) to the end of surgery was 23 minutes (SD 6) when isoflurane was used, and 22 minutes (SD 6) for oxygen alone.

Patients were assessed to have recovered immediately after isoflurane sedation. The surgeons' assessment (Table 1) in both procedures showed good operating conditions, with good patient cooperation, minor bleeding, absence of involuntary movements and gag reflex. The anaesthetists' assessment showed stable vital signs (Fig. 2) and positive

Table 1. Surgeons' assessment.

	Isoflurane	Oxygen
Cooperation of patient		
Good	13	13
Fair	0	0
Poor	0	0
Involuntary movements of tongue		
Nil	11	13
Occasional	1	0
Frequent	1	0
Gag reflex		
Nil	13	12
Occasional	0	1
Frequent	0	0
Bleeding		
Minor	12	13
Moderate	1	0

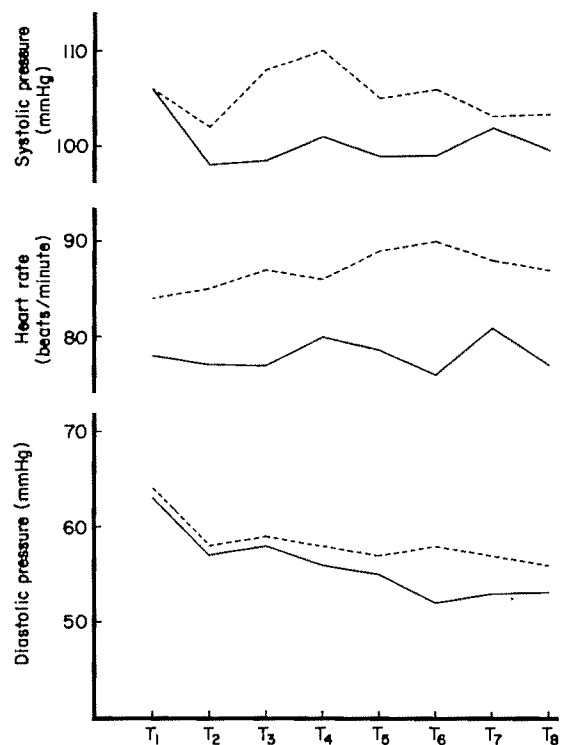


Fig. 2. Cardiovascular measurements before sedation (T₁), at optimum sedation (T₂), after local analgesic (T₃), during surgery (T₄–T₆), at end of surgery (T₇) and a few minutes after surgery (T₈). —, Isoflurane; ---, oxygen.

verbal response in both procedures. One patient complained of nausea during isoflurane sedation.

The number of patients who considered themselves to have been relaxed when questioned after local anaesthesia supplemented with isoflurane, was statistically significantly higher ($p < 0.005$) than after oxygen alone (Table 2). This was also true for those who slept during some of the procedure and for those who had amnesia for recall of events, although these differences were not significant. More patients had pain and discomfort when oxygen alone was used.

All patients except one detected an odour of the gas inhaled during isoflurane sedation. Four thought that the odour was pleasant and eight, unpleasant. All thought it was tolerable and thus none withdrew from the study.

Postoperative adverse effects (Table 3) were similar

Table 2. Patients' assessment following each operation.

	Isoflurane	Oxygen
Relaxation	13	4*
Sleep	6	0
Dreams	1	0
Pleasant	1	0
Unpleasant	1	0
Sexual	0	0
Amnesia for recall of events		
None	0	8
Partial	5	4
Complete	8	1
Amnesia for recall of pictures		
None	11	13
Partial	2	0
Complete	0	0
Pain	3	6
Discomfort	2	5
Odour		
Absent	1	13*
Pleasant	4	—
Unpleasant	8	—

* $p < 0.005$

Table 3. Postoperative adverse effects.

	Isoflurane		Oxygen	
	Patients	Average duration (days)	Patients	Average duration (days)
Drowsiness	5	2.0	4	1.2
Dizziness	7	1.4	3	1.0
Headache	7	1.9	1	1.0
Poor vision	1	1.0	1	1.0
Pain	12	4.0	11	3.5
Swelling	12	4.5	12	4.2
Bleeding	9	2.2	7	2.9
Insomnia	2	1.0	1	2.0
Nausea	2	1.5	2	1.5
Vomiting	0	0	0	0

Table 4. Patients' assessment after both procedures.

	Isoflurane	Oxygen	
Operation in which patient was more relaxed	11	2	($p < 0.005$)*
Preference	10	3	($p = 0.01$)*

* Fisher's exact probability test.

except for dizziness complained of by seven patients after isoflurane sedation compared to three after placebo. A significant majority ($p < 0.005$) said they were more relaxed with isoflurane sedation (Table 4), and a significant majority ($p = 0.01$) preferred isoflurane sedation to placebo.

Nitrous oxide

Twenty patients were included in the study, 11 males and 9 females. The age range was 18–31 years (mean 34, SD 3 years) and the weight range 43–70 kg (mean 56, SD 7 kg).

The dose of local anaesthesia used was similar during both isoflurane and nitrous oxide sedation. The duration of surgery when isoflurane was used for sedation, was 17 minutes (SD 6) and when nitrous oxide was used, 16 minutes (SD 6). The interval from the time of optimal sedation (10 minutes from the start of sedation) to the end

Table 5. Surgeons' assessment.

	Isoflurane	Nitrous Oxide
Sedation		
Light	0	1
Moderate	18	19
Deep	2	0
Cooperation of patient		
Good	17	19
Fair	3	1
Poor	0	0
Involuntary movements of tongue		
Nil	19	20
Occasional	1	0
Frequent	0	0
Gag reflex		
Nil	18	19
Occasional	2	0
Frequent	0	1
Bleeding		
Minor	19	20
Moderate	1	0

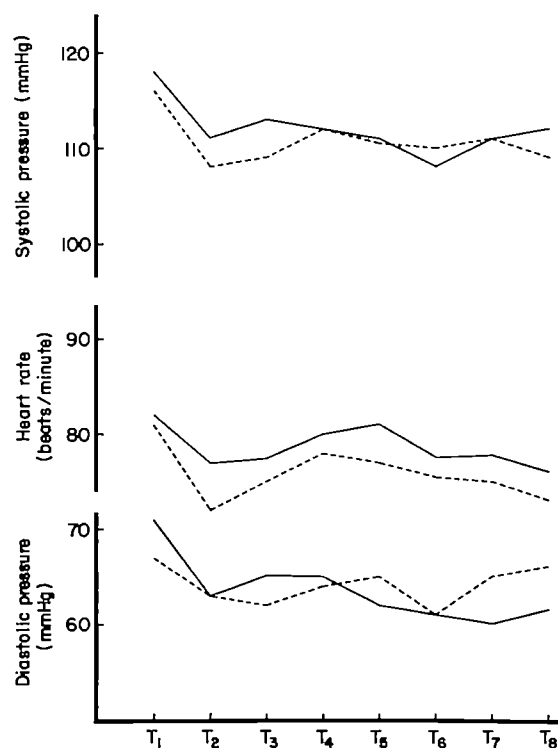


Fig. 3. Cardiovascular measurements before sedation (T₁), at optimum sedation (T₂), after local analgesic (T₃), during surgery (T₄–T₆), at end of surgery (T₇) and a few minutes after surgery (T₈). —, Isoflurane; ---, nitrous oxide.

of surgery was the same in both procedures, 23 minutes (SD 8).

Recovery following isoflurane sedation was immediate compared to 3 minutes (SD 8) with nitrous oxide sedation. The surgeons' assessment (Table 5) of both procedures showed moderate sedation and good operating conditions in the majority of patients, with good patient cooperation, minor bleeding, absence of involuntary movements of tongue and gag reflex. Two patients under isoflurane sedation were deeply sedated while one patient under nitrous oxide sedation was assessed to have light sedation.

Table 6. Patients' assessment following each operation.

	Isoflurane	Nitrous oxide
Relaxation	20	16
Sleep	10	7
Dreams	1	1
Pleasant	0	1
Unpleasant	0	0
Sexual	0	0
Amnesia for recall of events		
None	8	13
Partial	5	7
Complete	7	0
Amnesia for recall of pictures		
None	15	20
Partial	1	0
Complete	4	0
Pain	5	8
Discomfort	4	6
Odour		
Absent	5	7
Pleasant	3	5
Unpleasant	10	7
Neither	2	1

Table 7. Postoperative adverse effects.

	Isoflurane		Nitrous oxide	
	Patients	Average duration (days)	Patients	Average duration (days)
Drowsiness	7	1.7	10	2.1
Dizziness	2	1.5	6	2.1
Headache	6	2.3	9	2.3
Poor vision	2	1.0	2	1.5
Pain	15	3.6	17	3.2
Swelling	18	4.9	18	5.6
Bleeding	12	1.7	11	2.0
Insomnia	1	1.0	1	3.0
Nausea	0	0	4	1.2
Vomiting	0	0	2	1.0

Patient cooperation was assessed as fair in these three patients.

The anaesthetists' assessment showed stable vital signs (Fig. 3) and positive verbal response in both procedures. Verbal response was sluggish towards the end of the procedure in two cases under isoflurane sedation. One patient complained of irritation of the eyes due to the gas. One patient complained of numbness of the fingers during nitrous oxide sedation; two complained of nausea and one vomited towards the end of the procedure.

The majority of the patients when questioned after each procedure, said that they were relaxed (Table 6). A significant number said that they slept for some time during the procedure after both methods of sedation. Only one patient dreamt and no sexual dreams were reported. The number of patients who had amnesia for recall of events and recall of the picture cards, was greater after isoflurane sedation. Slightly more had pain and discomfort in the mouth after nitrous oxide sedation.

There was no significant difference between the numbers of patients who thought that they detected an odour in the gas that they were inhaling with the two methods. The majority thought that the odour was unpleasant but none withdrew from the study for this reason.

Postoperative adverse effects (Table 7) were similar except for the incidence of headache, dizziness, nausea and

Table 8. Patients' assessment after both procedures.

	Isoflurane	Nitrous oxide	
Operation in which patient was more relaxed	14	6	($\chi^2 = 4.9$, $p < 0.05$)*
Preference	15	5	($\chi^2 = 8.1$, $p < 0.01$)*

* Chi-square test.

vomiting, which was slightly higher after nitrous oxide sedation. However, the differences were not statistically significant.

A significant majority ($p < 0.05$) said that they were more relaxed with isoflurane sedation, and a significant majority ($p < 0.01$) said that they preferred isoflurane to nitrous oxide sedation (Table 8). Seventeen patients ($p < 0.01$) said that they would be willing to undergo sedation with both agents for future dental procedures. The other three patients did not wish to have sedation to supplement local anaesthesia. Two said that local anaesthesia was sufficient and one that he did not like the feeling of tiredness after the operation following sedation.

Discussion

It is important during outpatient surgical procedures to provide patient comfort.²⁸ Many techniques have been adopted to achieve this and inhalational sedation is one such technique. The inhalational agent commonly used is nitrous oxide; in this study 0.5% isoflurane was used for the same purpose. In a significant majority it provided better relaxation during the surgical procedure than either placebo or nitrous oxide. Furthermore, a significant majority preferred isoflurane when compared to placebo and nitrous oxide.

The irritating, pungent odour of isoflurane in anaesthetic concentrations causes patients to reject it as an induction agent, and produces coughing and laryngeal spasm. The majority of patients in this study thought that the odour was unpleasant but they tolerated it to the extent that a significant majority were willing to undergo isoflurane sedation at a future surgical procedure. Thus odour is not a problem with 0.5% isoflurane in oxygen. No coughing or laryngeal spasm was seen in any of these patients.

Blood pressure and heart rate in the first part of the study increased significantly above pre-operative levels during the procedure with 100% oxygen. These parameters did not increase above pre-operative levels in the second part of the study and were similar with both isoflurane and nitrous oxide sedation. The increase when surgery was done under local anaesthesia with 100% oxygen, indicates that although patients are cooperative, they are not relaxed. This is further highlighted by the fact that only four patients said that they were relaxed during the surgical procedure with 100% oxygen.

Verbal response was always present, though sluggish in two patients. Some patients said on questioning that they slept for some time during the procedure, but they responded easily to command. Relaxed patients close their eyes and their thoughts drift away,²⁹ which may be the reason for the above reply.

Anterograde amnesia is a beneficial property of a sedative used in traumatic procedures. Either partial or complete

amnesia for recall of events was exhibited by the majority after isoflurane sedation, and partial amnesia by some after both nitrous oxide sedation and oxygen. However, amnesia for recall of pictures shown at optimum sedation was exhibited only by some after isoflurane sedation. Thus, the partial amnesia exhibited by most patients was probably due to disinterest in the proceedings, once they were relaxed, rather than to an amnesic property of the drug.³⁰ The complete amnesia exhibited after isoflurane, especially for recall of objects, may have been due to a higher degree of sedation.

Patient cooperation was good in the majority regardless of the method of sedation, and involuntary movements of the tongue and the gag reflex were absent in the majority. Isoflurane in anaesthetic concentrations produces vasodilatation and may increase bleeding. However, this did not occur with the concentration used.

The isoflurane sedation was assessed as moderate in all cases except two, when it was assessed as deep. Anaesthetic assessment in these two patients showed that verbal response was present but sluggish towards the end of the procedure. The duration of isoflurane sedation in this study was in the range 22–46 minutes from the beginning of inhalation. Thus the period of sedation was relatively short. However, it remains to be investigated whether a patient may lose verbal contact in prolonged procedures under sedation with 0.5% isoflurane in oxygen. It is better to reduce the inspired concentration if verbal contact becomes sluggish and it should be switched off if verbal contact is lost, and surgery stopped until the patient regains verbal response. A lower concentration of isoflurane should then be used.

Quick recovery is one of the advantages of inhalational sedation with nitrous oxide.³⁰ In this study recovery was rapid even with 0.5% isoflurane in oxygen. Recovery was tested thoroughly: patients were made to ascend and descend a flight of stairs, and dizziness was assessed before they were discharged. However, it must be noted that patients were allowed to breathe 100% oxygen for 10 minutes before recovery was tested.

Postoperative adverse effects with nitrous oxide sedation have been reported to be similar to those without nitrous oxide.³⁰ The incidence of postoperative adverse effects with isoflurane was similar to that with placebo in this study, except for a greater number of reports of headache and dizziness. However, the number of patients who had both headache and dizziness was greater following nitrous oxide sedation and the incidence of nausea and vomiting was also slightly higher.

In conclusion, this study shows that 0.5% isoflurane in oxygen has no major disadvantages over nitrous oxide sedation. It appears to have advantages in that isoflurane is not reported to interfere with vitamin B₁₂ metabolism or to be associated with abortions. A significant proportion of the patients in this study preferred isoflurane to nitrous oxide sedation. These findings justify further investigation of isoflurane sedation with the aim of incorporating it into clinical practice.

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References

1. WYLIE WD. Report of the working party on training in dental anaesthesia, para 8. *Report of an interfaculty working party on training in dental anaesthesia*. Royal College of Surgeons, England, October 1981.
2. COLEMAN AJ. Inhalational anaesthetic agents. In: Churchill-Davidson HC, ed. *A practice of anaesthesia*, 4th ed. London: Lloyd-Luke, 1978: 242.
3. MUNSON ES, EGER EI II, THAM MK, EMBRO WJ. Increase in anaesthetic uptake, excretion, and blood solubility in man after eating. *Anaesthesia and Analgesia* 1978; **57**: 224–31.
4. EVERETT GB, ALLEN GD. Simultaneous evaluation of cardiorespiratory and analgesic effects of nitrous oxide–oxygen inhalation analgesia. *Journal of the American Dental Association* 1971; **83**: 129–33.
5. ALLEN GD. *Dental analgesia. Postgraduate dental handbook series, Vol. 6*. Littleton, MA: PSG Publishing Company, 1979.
6. PARBROOK GD, REES GAD, ROBERTSON GS. Relief of post-operative pain: comparison of a 25% nitrous oxide and oxygen mixture with morphine. *British Medical Journal* 1964; **2**: 480–2.
7. NUNN JF. Clinical aspects of the interaction between nitrous oxide and vitamin B₁₂. *British Journal of Anaesthesia* 1987; **59**: 3–13.
8. SWEENEY B, BINGHAM RM, AMOS RJ, PETTY AC, COLE PV. Toxicity of bone marrow in dentists exposed to nitrous oxide. *British Medical Journal* 1985; **291**: 567–9.
9. LAYZER RB. Myeloneuropathy after prolonged exposure to nitrous oxide. *Lancet* 1978; **2**: 1227–30.
10. COHEN EN, BELLVILLE JW, BROWN BW. Anesthesia, pregnancy and miscarriage. A study of operating room nurses and anaesthetists. *Anesthesiology* 1971; **35**: 343–7.
11. COHEN EN, BROWN BW, BRUCE DL, CASCORBI HF, CORBETT TH, JONES TW, WHITCHER CE. American Society of Anesthesiologists Ad Hoc Committee. Occupational disease among operating room personnel: a national study. *Anesthesiology* 1974; **41**: 321–40.
12. COHEN EN, GIFT HC, BROWN BW, GREENFIELD W, WU ML, JONES TW, WHITCHER CE, DRISCOLL EJ, BRODSKY JB. Occupational disease in dentistry and chronic exposure to trace anesthetic gases. *Journal of the American Dental Association* 1980; **101**: 21–31.
13. EDMUNDS DH, ROSEN M. Inhalation sedation for conservative dentistry. A comparison between nitrous oxide and methoxyflurane. *British Dental Journal* 1975; **139**: 398–402.
14. DRAGON A, GOLDSTEIN I. Methoxyflurane: preliminary report on analgesic and mood-modifying properties in dentistry. *Journal of the American Dental Association* 1967; **75**: 1176–81.
15. COUSINS MJ, MAZZE RI. Methoxyflurane nephrotoxicity; a study of dose response in man. *Journal of the American Medical Association* 1973; **225**: 1611–6.
16. COUSINS MJ, MAZZE RI, KOSEK JC, HITT BA, LOVE FV. The etiology of methoxyflurane nephrotoxicity. *Journal of Pharmacology and Experimental Therapeutics* 1974; **190**: 530–41.
17. COHEN EN. Toxicity of inhalation anaesthetic agents. *British Journal of Anaesthesia* 1978; **50**: 665–75.
18. CROMWELL TH, EGER EI II, STEVENS WC, DOLAN MW. Forane uptake, excretion, and blood solubility in man. *Anesthesiology* 1971; **35**: 401–8.
19. HOLADAY DA, FISEROVA-BERGEROVA V, LATTO IP, ZUMBIEL AM. Resistance of isoflurane to biotransformation in man. *Anesthesiology* 1975; **43**: 325–32.
20. COUSINS MJ, GREENSTEIN LR, HITT BA, MAZZE RI. Metabolism and renal effects of enflurane in man. *Anesthesiology* 1976; **44**: 44–53.
21. EGER EI II. The pharmacology of isoflurane. *British Journal of Anaesthesia* 1984; **56** (Suppl.): 71S–99S.
22. EGER EI II. *Isoflurane (Forane): a compendium and reference*. Madison, WI: Ohio Medical Products, 1981.
23. CROMWELL TH, STEVENS WC, EGER EI II, SHAKESPEARE TF, HALSEY MJ, BAHLMAN SH, FOURCADE HE. The cardiovascular effects of compound 469 (Forane) during spontaneous ventilation and CO₂ challenge in man. *Anesthesiology* 1971; **35**: 17–25.

24. FOURCADE HE, STEVENS WC, LARSON CP Jr, CROMWELL TH, BAHLMAN SH, HICKEY RF, HALSEY MJ, EGER EI II. The ventilatory effects of Forane, a new inhaled anesthetic. *Anesthesiology* 1971; **35**: 26-31.
25. STEVENS WC, DOLAN WM, GIBBONS RT, WHITE A, EGER EI II, MILLER RD, DE JONG RH, ELASHOFF RM. Minimum alveolar concentrations (MAC) of isoflurane with and without nitrous oxide in patients of various ages. *Anesthesiology* 1975; **42**: 197-200.
26. WINTER PM, HORNBEIN TF, SMITH G. Hyperbaric nitrous oxide anesthesia in man: determination of anesthetic potency (MAC) and cardiorespiratory effects. *Annual Meeting of the American Society of Anesthesiologists* 1972; *Abstracts of Scientific Papers*: 103-4.
27. ALBUM B, OLSEN I, LOKKEN P. Bilateral surgical removal of impacted mandibular third molar teeth as a model for drug evaluation: a test with oxyphenbutazone (Tanderil). *International Journal of Oral Surgery* 1977; **6**: 177-89.
28. LUNGREN S, ROSENQUIST JB. Comparison of sedation, amnesia and patient comfort produced by intravenous and rectal diazepam. *Journal of Oral and Maxillofacial Surgery* 1984; **42**: 646-50.
29. RODRIGO MRC, CHEUNG LK. Oral midazolam sedation in third molar surgery. *International Journal of Maxillofacial Surgery* 1987; **16**: 333-7.
30. RODRIGO MRC. A study of inhalational sedation with nitrous oxide/oxygen for oral surgery in Hong Kong Chinese. *Annals of the Academy of Medicine, Singapore* 1986; **15**: 315-9.

CASE REPORT

Reversal of sedation by prolonged infusion of flumazenil (Anexate, Ro 15-1788)

A. BODENHAM, G. BROWNLIE, J. S. DIXON AND G. R. PARK

Summary

A 22-year-old male was involved in a road traffic accident and sustained multiple injuries. He received an infusion of midazolam to sedate him during a period of artificial ventilation. His conscious level remained depressed 36 hours after the infusion was discontinued but the sedation was completely reversed with flumazenil. An infusion was started because of the short duration of action of flumazenil, and continued for 8 days. The infusion was stopped seven times during this period and on each occasion except the last, his conscious level deteriorated but returned to normal when flumazenil was administered again. Plasma concentrations of midazolam and α -hydroxymidazolam were measured and found to be low during this period. Possible explanations for this finding are discussed.

Key words

Hypnotics, benzodiazepines; midazolam.

Antagonists, benzodiazepines; flumazenil.

Midazolam is frequently used to produce sedation in critically ill patients. It is metabolised to α -hydroxymidazolam, which is also thought to be active in man. We report a patient in whom prolonged sedation was seen after a midazolam infusion. The sedation was reversible with the benzodiazepine antagonist flumazenil (Anexate, Ro 15-1788), which is commercially available in most of Europe but currently available only on a named-patient basis in Great Britain.

Case history

A 22-year-old male, weight approximately 110 kg, was transferred to this intensive care unit for artificial ventilation of the lungs, intermittent haemodialysis and continuous arteriovenous haemofiltration. He was involved in a road traffic accident 3 days previously in which he sustained a fractured pelvis and femur and had also avulsed his left kidney from its vascular pedicle. He had avulsed his right kidney in a similar accident 4 years previously and this had necessitated surgical removal.

The patient required artificial ventilation of the lungs for pulmonary oedema on admission to the unit, and large amounts of sedation and analgesia were necessary to allow this. These requirements were met initially with bolus doses of midazolam and fentanyl and subsequently by intravenous infusion of both drugs.

He required a total of 800 mg midazolam and 3.3 mg fentanyl over a period of 5 days (Fig. 1). His breathing was adequate but he remained sleepy 24 hours after their discontinuation. The patient did not tolerate the tracheal tube and this was therefore removed. His neurological status was unchanged 12 hours after extubation and this was attributed to accumulation of midazolam. His cough reflex was depressed at this time and he had developed sputum retention. Small intravenous boluses of flumazenil, to a total dose of 0.5 mg, were given which produced a rapid but short-lived improvement in his conscious level and ability to cough. This was followed by an infusion of flumazenil at a rate of 0.5 mg/hour, which maintained both full consciousness and the ability to cough spontaneously. In addition, a naloxone infusion 0.2 mg/hour was started 12 hours later and continued for 48 hours to reverse any residual opioid effects.

The flumazenil infusion was continued for 8 days. It was discontinued seven times in this period and on each occasion except the last, the patient became unconscious, responded only to painful stimuli and then awoke within 60 seconds after he received a 0.5 mg bolus of flumazenil. He was noted to sleep normally for up to 3 hours at any one time during the flumazenil infusion, although his sleep pattern was disturbed by his stay in the intensive care unit.

He no longer required flumazenil to maintain conscious-

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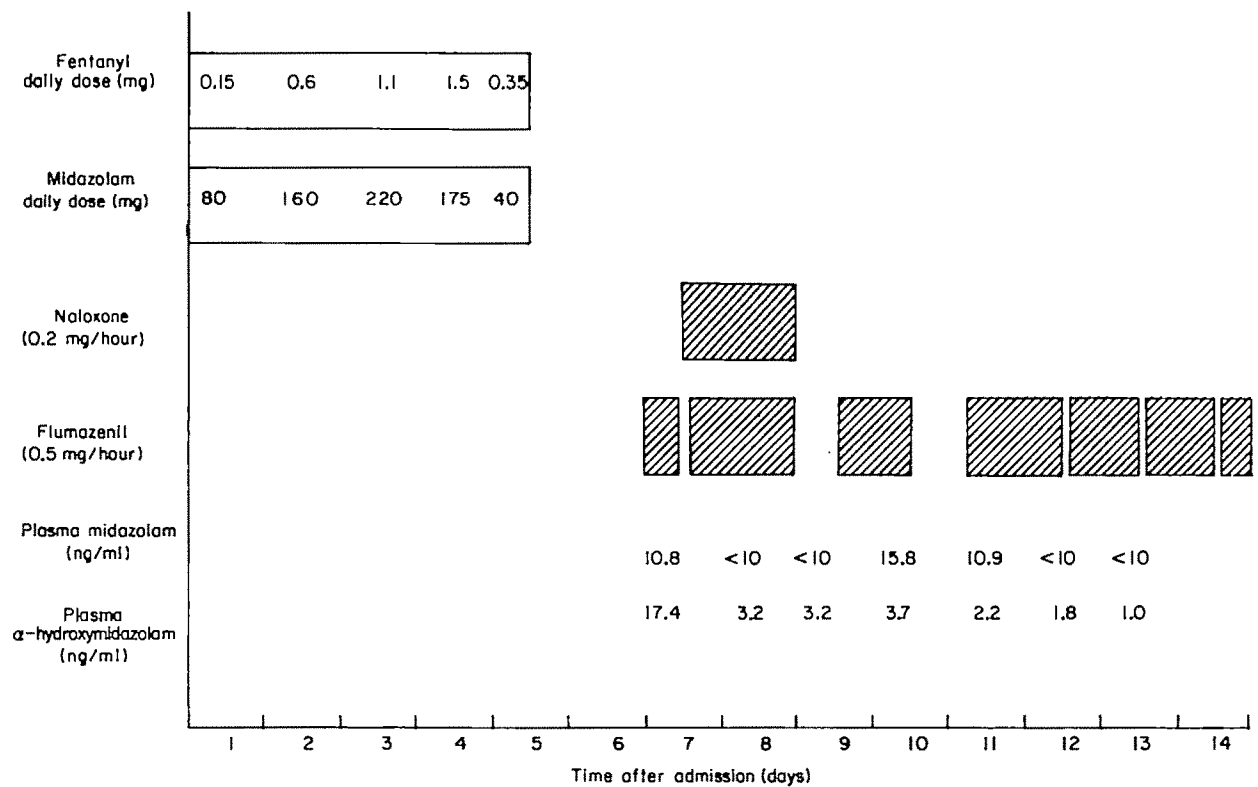


Fig. 1. Daily dosages of midazolam and fentanyl and their respective antagonists naloxone and flumazenil. Plasma concentrations of midazolam and α -hydroxymidazolam.

ness 10 days after the sedation was stopped and he began a long convalescence and still required renal dialysis.

Samples of plasma were collected on days 7–13 for estimation of concentrations of midazolam and α -hydroxymidazolam by validated gas–liquid chromatography,¹ with an accuracy of $\pm 10\%$ and a precision of $<7\%$.

Discussion

This patient required large and frequent doses of sedatives and analgesics to facilitate intensive care; these might have been related to his age, weight and ethanol consumption. Fentanyl or alfentanil are the opioids of choice in patients with renal failure due to their lack of accumulation and active metabolites, in contrast to morphine² and pethidine.³ Midazolam has been shown to have a prolonged elimination in critically ill patients⁴ and this may be due to a reversible failure of metabolism⁵ or to a pharmacogenetic abnormality.⁶

Flumazenil is thought to be a specific benzodiazepine receptor antagonist. It has been shown to be a safe agent for the reversal of benzodiazepine sedation in patients who require intensive care.⁷ Few adverse effects have been seen except for nausea and vomiting. Fears about convulsions on rapid awakening have not been realised and, paradoxically, flumazenil has been shown to have intrinsic anticonvulsant properties.⁸ However, the dose must be titrated against the patient's response if adverse cardiovascular responses similar to those seen after naloxone⁹ are to be avoided. Cardiovascular instability has not been reported in studies to date.¹⁰ A short elimination half-life (one hour) may necessitate repeated bolus doses or an

infusion in cases of significant benzodiazepine accumulation.

The flumazenil infusion was necessary to keep the patient fully awake and able to cough and its use prevented the need for tracheal intubation and assisted ventilation. Any residual effects of opioids in this patient were reversed by the infusion of naloxone, which confirms that the arousal produced by flumazenil was not due to a nonspecific action in opioid reversal.

Analysis of samples showed low plasma concentrations of midazolam and its metabolite on days 7–13 (Fig. 1). α -Hydroxymidazolam is an active metabolite with a short half-life and sedation in healthy subjects correlates best with combined levels of midazolam and this metabolite. The combined midazolam and α -hydroxymidazolam concentrations in this patient were lower than the 30–100 ng/ml needed to produce sedative effects in healthy volunteers.¹¹ Larger doses over a period of days may cause significant accumulation of lipid soluble midazolam within the central nervous system and elsewhere which may not be reflected in plasma concentrations.

The arousal action of flumazenil in the face of low plasma concentrations of benzodiazepines suggests firstly that plasma concentrations do not reflect those at the receptors within the central nervous system after prolonged administration of the drug. Plasma concentrations of the drug were first measured 7 days after the infusion was started, when high tissue levels could have developed which would diffuse only slowly back into the plasma for subsequent elimination. Secondly, flumazenil may have non-specific analeptic properties, similar to doxapram, but the patient's ability to sleep whilst on the infusion suggests that

this is not its mode of action. Thirdly, receptor changes may occur in disease states which alter the response to a given dose of midazolam. Finally, anecdotal reports have suggested that flumazenil may reverse some features of hepatic encephalopathy, mediated via the GABA system.¹² This raises the possibility that changes in GABA neurotransmitters may be involved with the encephalopathy of acute metabolic disease¹³ and flumazenil may reverse this.

Plasma concentrations of benzodiazepines may yield valuable pharmacokinetic and pharmacodynamic information in single dose studies and during short periods of sedation and anaesthesia in healthy patients. Their interpretation in critically ill patients is difficult since very little published information is available. The importance of active metabolites remains to be determined.⁵ It appears unwise to base clinical decisions on the presence of high or low plasma concentrations of midazolam or α -hydroxy-midazolam until further information is available. The need for caution in the interpretation of plasma concentrations applies to other benzodiazepines used in critically ill patients.

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References

1. HEINZMANN P, VON ALTEN R. Determination of midazolam and its α -hydroxy-metabolite in plasma by gas chromatography with electron capture detection. *Journal of High Resolution Chromatography and Chromatography Communications* 1981; **4**: 266-9.
2. OSBORNE RJ, JOEL SP, SLEVIN ML. Morphine intoxication in renal failure: the role of morphine 6 glucuronide. *British Medical Journal* 1986; **292**: 1548-9.
3. SZETO HH, INTURRISI CE, HOUDE R, SAAL S, CHEIGH J, REIDENBERG MM. Accumulation of normeperidine, an active metabolite of meperidine, in patients with renal failure or cancer. *Annals of Internal Medicine* 1977; **86**: 738-41.
4. BYATT CM, LEWIS LD, DAWLING S, COCHRANE GM. Accumulation of midazolam after repeated dosage in patients receiving mechanical ventilation in an intensive care unit. *British Medical Journal* 1984; **289**: 799-800.
5. SHELLY MP, MENDEL L, PARK GR. Failure of critically ill patients to metabolise midazolam. *Anaesthesia* 1987; **42**: 619-26.
6. DUNDEE JW, COLLIER PS, CARLISLE RJT, HARPER KW. Prolonged midazolam elimination half-life. *British Journal of Pharmacology* 1986; **21**: 425-9.
7. KLEINBERGER G, GRIMM G, LAGGNER A, DRUME W, LENZ K, SCHNEEWEISS B. Weaning patients from mechanical ventilation by benzodiazepine antagonist Ro 15-1788. *Lancet* 1985; **2**: 268-9.
8. SCOLLO LAVIZZARI G. The anticonvulsant effect of the benzodiazepine antagonist, Ro 15-1788: an EEG study in 4 cases. *European Neurology* 1984; **23**: 1-6.
9. SMITH G, PINNOCK C. Editorial. Naloxone—paradox or panacea? *British Journal of Anaesthesia* 1985; **57**: 547-9.
10. GELLER E, CHERNILAS J, HALPERN P, NIV D, MILLER HI. Hemodynamics following reversal of benzodiazepine sedation with Ro 15-1788 in cardiac patients. *Anesthesiology* 1986; **61**: A49.
11. CREVOISIER C, ZIEGLER WH, ECKERT M, HEIZMANN P. Relationship between plasma concentration and effect of midazolam after oral and intravenous injection. *British Journal of Clinical Pharmacology* 1983; **16**: 51S-61S.
12. SCOLLO-LAVIZZARI G, STEINMANN E. Reversal of hepatic coma by benzodiazepine antagonist (Ro 15-1788). *Lancet* 1985; **1**: 1324.
13. PLUM F, POSNER JB. The diagnosis of stupor and Coma. Philadelphia: F.A. Davis, 1980: 206-7.

CASE REPORT

Overtransfusion as a possible cause of split skin graft loss

G. W. G. FRENCH AND P. TOMLINSON

Summary

A child who underwent burns surgery received excessive transfusion of red blood cells during operation and subsequently suffered severe skin graft and donor site loss. The possible causes are discussed and hyperviscosity is suggested to be the most probable.

Key words

Blood; viscosity, replacement.

Surgery; plastic.

Case history

A previously healthy, one-year-old boy (weight 9 kg) overturned an electric fat fryer and was burned with hot oil. He sustained a 24% mixed depth burn to the areas shown in Fig. 1.

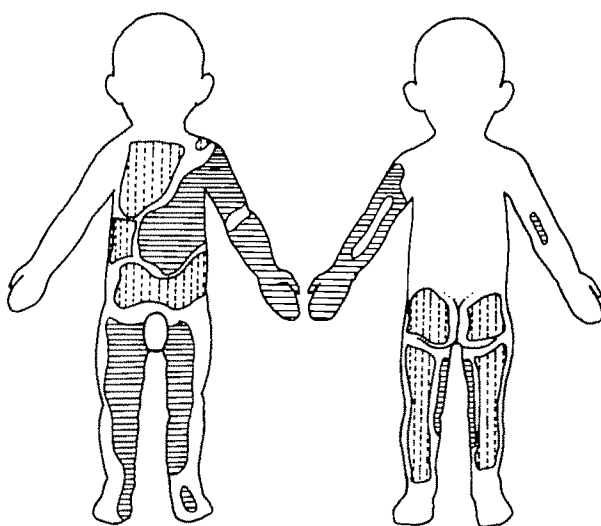


Fig. 1. Areas of burn and donor sites on child (left, anterior; right, posterior). ■, Burn sites; □, donor sites.

He was resuscitated during the shock phase with plasma protein fraction, using an adaptation of the Muir and Barclay formula.¹ Crystalloid requirements were given as 4% dextrose–0.18% saline intravenously. Compound sodium chloride and glucose oral powder (Dioralyte) were given when he could tolerate oral fluids. He came through the first 48 hours uneventfully.

The Nottingham Burns Unit has adopted the technique of early tangential shaving and grafting² and his chest and left arm burns were shaved and mesh-grafted³ on the fifth day after admission. He was returned to theatre on day 9, his leg burns were debrided and dressed and further split skin grafts were harvested and stored.

His previous grafts were also inspected. There was complete loss of graft from recipient sites on his chest and left arm, and both recipient and donor sites showed widespread necrosis. The donor bed, which should have been pink with healthy re-epithelialisation, was black and necrotic; not only was there no repair, but there was loss of the dermal latticework which is normally left after split skin harvesting.⁴ The recipient bed on the arm and chest showed necrosis of both the fat and dermal remnants. The bed would normally be beginning to sprout healthy pink granulation tissue at this stage. The split skin graft would also be 'pinking up' and sticking down to its bed. Instead, it was shrivelled up and black; it still lay on the areas where it had been applied but was mobile.

This pattern had not been seen in the burns unit before and was difficult to explain. There was no family history of skin or collagen disorders, and histological examination of the burned areas revealed only a non-specific, chronic, mid-dermal perivascular infiltrate. The child was treated conservatively for a further 2 weeks with topical silver sulphadiazine 1% cream and povidone-iodine solution 10%. Subsequent grafting was successful, both to the original burn sites and to the necrotic donor areas.

He was discharged to outpatient care 8 weeks after his burn and is now being treated for scar contractures and thickening. These would undoubtedly have been less severe

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had the first grafts taken. The scarring on his donor sites is also worse than average.

Discussion

There are several possible causes of graft failure in this patient.

Fat necrosis. Inadequate shaving and debridement of burned tissue, with consequent fat necrosis, can predispose to patchy graft loss. However, both surgeons were experienced in burns surgery and each was satisfied that healthy fat had been exposed. Furthermore, inadequate debridement does not explain the donor site necrosis. Donor sites are normally fully healed within 10–14 days.

Infection. This is one of the commonest causes of skin graft loss. The child had a rectal temperature of 38.0–38.5°C on many occasions in the first 10 days of his illness. A pyrexia of this order is very common in burns patients and often persists until the burn heals or is grafted. Antipyretics (acetyl salicyclic acid and ibuprofen) were administered intermittently whilst the results of bacteriological investigations were awaited. His condition remained stable.

Swabs and punch biopsies were taken regularly throughout his illness, and the following organisms grown: *Staphylococcus aureus*, Coliform bacilli, *Enterococci* and *Acinetobacter anitratus*. Blood cultures were negative for bacteria, viruses and fungi. None of these organisms is a common cause of serious graft loss^{4,5} either individually or synergistically. Graft loss is often associated with *Streptococci* of the Lancefield group A.⁶ This organism was not found and there was no pus or evidence of an excessively wet wound.

Coagulation disorders. Excessive clot formation under grafts is a recognised cause of graft failure. There was no evidence that the child suffered from any familial clotting disorder and there was very little postoperative blood loss. However, a greater amount of bleeding occurred in theatre than was expected (see below) and this was probably the cause of the low platelet count immediately post-operatively (Table 1). A clotting screen performed on day 6 was normal and no increase in fibrin degradation products was found.

The ibuprofen and acetyl salicyclic acid which were given pre-operatively are known to decrease platelet adhesiveness⁷ but the minimal postoperative blood loss probably excludes these drugs as significant causes of graft failure.

Shearing. The grafts were fixed to the recipient sites with cyanoacrylate cement around their edges, and were still *in situ* at day 9, although necrotic. Small areas of loss may occur directly under the cement but this would not explain the generalised necrosis.

Malnutrition. The child was well nourished on admission and had had no significant past or recent illness. However, occasional vomiting, diarrhoea and inadequate nutritional intake necessitated supplementary feeding from day 3. Enteral feeding via a small bore nasogastric tube was replaced by intravenous feeding on day 14. The child's nutritional needs were calculated using the Sutherland formula.⁸

Grafts applied upside down. The grafts were applied to the recipient sites in strips of around 5 × 10 cm and it is inconceivable that all of them were positioned upside down to account for the observed uniform loss. All the theatre staff were highly skilled in burns surgery and it is rare for even one piece of skin to be applied wrongly.

Thickness of graft. Thin split skin grafts are associated with a lower failure rate than thick ones. However, an electric dermatome was used to harvest skin in this child; this device cuts consistently thin grafts. In addition, necrosis of the donor site cannot be explained by the thickness of the graft.

Overtransfusion. The preoperative haemoglobin concentration was 8.7 g/dlitre (Table 1). The child was estimated to have lost 1350 ml of blood in theatre during the first operation. The estimate was based on swab weighing and an assessment of the amount of blood lost on the drapes. Consequently, he was transfused with 1500 ml of fresh whole blood, to minimise the complications which stored blood might have caused.⁹

A routine haematocrit on return to the ward, was found to be 53% (normal 38%) and signs of venous stasis were apparent on his face and trunk. Other parameters such as blood pressure, urine output and hydration were considered to be satisfactory so venesection was performed; 80 ml of blood were removed and his haematocrit decreased to 46% one hour later. His haemoglobin was 15 g/dlitre on the first postoperative day. All other investigations were normal.

Blood viscosity increases exponentially with packed cell volume.¹⁰ The viscosity is lower in vessels less than 200 µm in diameter (capillaries, arterioles and venules) (Fahraeus–Lindqvist effect);¹¹ capillary readings are normally around 10% lower than those in large vessels. However, viscosity in the small vessels increases in low flow states. This 'anomalous viscosity' is due not only to the loss of axial streaming but also to rouleaux formation by the red cells. Thus, sludging in the microcirculation causes severe resistance to flow and may result in tissue ischaemia.

In this patient, there was a 92% increase in relative viscosity of blood after operation (from 2.5 to 4.8; Table 1). We believe that this may have reduced the flow of blood to the healing epithelium of the donor site, the ingrowing

Table 1. Laboratory investigations.

	Time after burn (days)					
	4	5	5 (after operation)	6	7	11
Haemoglobin (g/dlitre)	10.0	8.7	17.1	15.7	14.0	14.4
White cell count (× 10 ⁹ /litre)	2.5	2.6	7.2	7.9	11.2	18.3
Platelet count (× 10 ⁹ /litre)	195	173	38	26	38	242
Haematocrit (%)	30	26	53	46	41	42
Relative viscosity*	2.7	2.5	4.8	4.0	3.5	3.6
Albumin (g/litre)	—	24	—	—	—	20

* Viscosity relative to water, which is measured as 1.0 cP (centipoise).

capillaries of the recipient sites and the split skin graft to such an extent that widespread necrosis resulted.

Accurate estimation of blood loss in theatre is critical if overtransfusion is to be avoided. Tangential shave and grafting often leaves an exposed, bleeding surface unless a tourniquet is used. The haemorrhage continues until the graft is laid on and blood loss is often extensive. It is easy to misinterpret results of swab weighing, especially when topical irrigating solutions (e.g. hydrogen peroxide) are applied prior to the application of skin grafts. Furthermore, attempts in theatre to correct apparent pre-operative anaemias add to the difficulties of assessing transfusion requirements.

In conclusion, we believe that overtransfusion during the operative period was the most likely cause of split skin graft loss in this child. Careful assessment of pre-operative anaemia and blood loss is essential in the management of these patients. A relative anaemia (e.g. 10 g/dlitre) with optimal viscosity might be preferable in the postoperative period.

References

1. MUIR IFK, BARCLAY TL. *Burns and their treatment*. London: Lloyd Luke, 1974; 30.
2. JANZEKOVIC Z. A new concept in the excision and immediate grafting of burns. *Journal of Trauma* 1970; **10**: 1103-8.
3. MACMILLAN BG. The use of mesh grafting in treating burns. *Surgical Clinics of North America* 1970; **6**: 1347-59.
4. MCGREGOR IA, ed. *Fundamental techniques of plastic surgery*, 7th edn. Edinburgh: Churchill Livingstone, 1980; 55-99.
5. CASON JS. Skin grafting. In: CASON JS, ed. *Treatment of burns*. London: Chapman and Hall, 1981: 108-41.
6. LIEBERG NCF, KUHN LR, BARNES BA, REISS E, AMSPACHER WH. Infection in burns. II. The pathogenicity of streptococci. *Surgery, Gynecology and Obstetrics* 1954; **98**: 693-9.
7. GLENN EM, BOWMAN BJ. In vitro effects of non-steroidal anti-inflammatory drugs (NAIFD). *Proceedings of the Society of Experimental Biology and Medicine* 1969; **130**: 1327-32.
8. SUTHERLAND AB. Nitrogen balance and nutritional requirements in the burn patient. *Burns* 1976; **2**: 238-44.
9. MILLER RD. Complications of massive blood transfusions. *Anesthesiology* 1973; **39**: 82-93.
10. SMITH JJ, KAMPINE JP. Hemodynamics. In: SMITH JJ, KAMPINE JP, eds. *Circulatory physiology—the essentials*, 2nd edn. Baltimore: Williams and Wilkins, 1984; 16-31.
11. FAHRAEUS R, LINDQVIST T. The viscosity of blood in narrow capillary tubes. *American Journal of Physiology* 1931; **96**: 562-8.

CASE REPORT

Macroglossia and posterior fossa disease

J. K. MOORE, S. CHAUDHRI, A. P. MOORE AND J. EASTON

Summary

We describe five cases of macroglossia in patients with posterior fossa disease and suggest that the primary mechanism is neurogenically determined rather than one of vascular obstruction or local trauma.

Key words

Anaesthesia; neurosurgical.

Complications; macroglossia.

Macroglossia was reported in five patients as a complication of posterior fossa surgery in the sitting position.^{1–5} The authors considered that the cause was either local trauma or venous obstruction related to the use of the sitting position.

We report four patients who developed macroglossia after posterior fossa exploration in whom the sitting position cannot be implicated. A fifth patient with a high cervical cord and brain stem tumour developed macroglossia during the last 2 weeks of life. The aetiology of this rare complication may not be as straightforward as was previously thought: our experience suggests a possible neurogenic origin.

Case histories

Case 1

A 27-year-old woman presented with an 18-month history of progressive ataxia, unilateral deafness and headache and was found to have bilateral acoustic neuromas and hydrocephalus. Preliminary insertion of a ventriculoperitoneal shunt was uneventful.

Definitive surgery was performed 4 weeks later. The trachea was intubated with an armoured orotracheal tube after induction of anaesthesia. A nasogastric tube was passed and a throat pack loosely inserted but an oral airway was not used. A central venous catheter was inserted via the right internal jugular vein. The patient was placed in the park bench position using a Gardner headrest. There was only moderate flexion of the neck; the chin was two fingers' breadth above the chest.

A combined right temporal craniotomy with right lateral posterior fossa craniectomy was performed and the larger

tumour resected. It was necessary to remove the lateral third of the cerebellum to minimise the degree of retraction needed to remove the tumour completely. The ninth to twelfth cranial nerves were preserved but the facial nerve could not be separated from the tumour mass. The surgical field was good with no evidence of venous congestion. Anaesthesia lasted for 14 hours and was uneventful; induced hypotension was not used.

The patient rapidly became intolerant of the tracheal tube postoperatively and the trachea was extubated. Sudden respiratory arrest occurred half an hour later without prior respiratory obstruction. Her trachea was easily re-intubated and the larynx and pharynx appeared normal. No surgically remediable cause was identified by computerised axial tomography (CAT scan) so her lungs were ventilated overnight.

Her tongue was very swollen, firm and red 8 hours postoperatively and protruded 3 cm from the mouth (Fig. 1). She was afebrile, responded to commands and had a normal respiratory pattern. The tongue remained massively enlarged over the next few days and was painful, which made oral toilet difficult. She developed an ulcerated area on the tongue from pressure of the teeth which was treated by the insertion of bilateral bite blocks, and a tracheostomy was performed on the sixth postoperative day. The swelling resolved by the fourteenth postoperative day and the patient subsequently recovered completely apart from facial weakness and deafness.

Case 2

A 32-year-old man developed signs of elevated intracranial pressure. CAT scan showed a large left acoustic neuroma.

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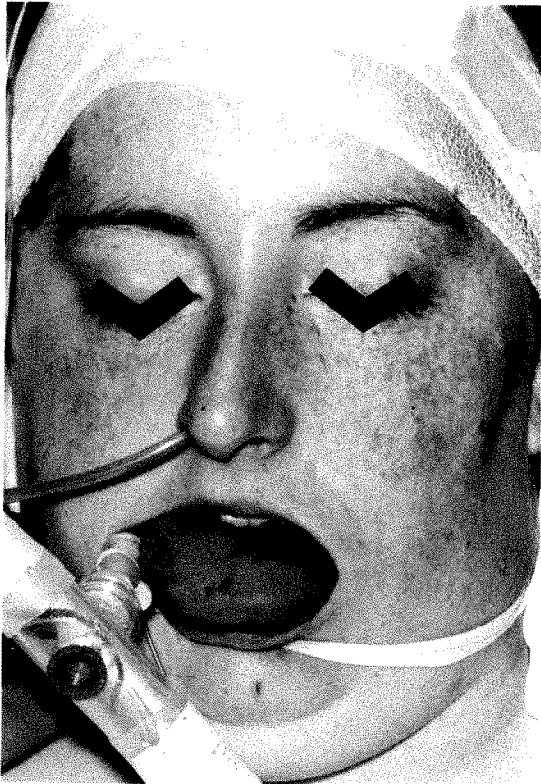


Fig. 1. Macroglossia in patient 1.

A ventriculoperitoneal shunt was inserted and definitive surgery was performed 2 weeks later. Anaesthesia was uneventful; an orotracheal tube and throat pack were used but not an oral airway. The patient was operated on in the park bench position. Complete tumour excision was achieved but this required division of the seventh and eighth cranial nerves. The operation lasted 12 hours and the patient's trachea was extubated promptly postoperatively. He developed acute respiratory obstruction 8 hours later, due to swelling of the tongue. An attempt was made to re-intubate his trachea under general anaesthesia but this failed and an emergency tracheostomy was performed. The tongue continued to swell for 4 days and then began to improve. The swelling resolved completely after 2 weeks.

Case 3

A 54-year-old woman who had a history of partial resection of a middle fossa meningioma 5 years earlier, now presented with palsies of the right cranial nerves III, IV, V, VIII, IX and X. CAT scan and magnetic resonance imaging showed a new posterior fossa meningioma. Surgery was carried out in the park bench position and the meningioma, which extended from the jugular foramen to the tentorial hiatus, was resected. Anaesthesia was uneventful; an armoured orotracheal tube and throat pack were used but not an oral airway. The procedure lasted 8 hours with a smooth initial recovery. However, she developed swelling of the tongue and face 36 hours postoperatively and had several episodes of stridor. She was treated conservatively with humidified oxygen-enriched air and the macroglossia resolved over the next few days. Her cranial nerve function was unchanged.

Case 4

A 24-year-old man with a family history of neurofibromatosis presented with bilateral acoustic neuromas. The smaller tumour on the left was resected in June 1985 and he then had radiotherapy to the right-sided tumour. The right-sided tumour required surgery in 1987 because of increasing deafness. The trachea was intubated with a non-armoured orotracheal tube after induction of anaesthesia and a throat pack inserted loosely. Surgery was again performed in the park bench position. A three-point headrest was used and there was marked neck flexion. Complete tumour excision was achieved but the VIIth nerve and vestibular branch of the VIIIth nerve were divided. Venous congestion was apparent during surgery but repositioning of the head was not possible. Anaesthesia lasted for 12 hours.

The patient's trachea was not extubated postoperatively because immediately the pack was removed the tongue began to swell until it protruded 2–3 cm from the mouth. Tracheostomy was performed on the second day. The tongue was again exquisitely painful and this was managed with topical lignocaine. Dexamethasone was given in an attempt to minimise swelling but it resolved only after 13 days.

Case 5

A 48-year-old woman complained of neck pain and over 4 weeks developed hemiplegia. She had an episode suggestive of optic neuritis 13 years earlier. Magnetic resonance imaging was consistent with an intramedullary tumour or demyelination from C₂ to C₄. She deteriorated despite treatment with steroids and azathioprine and required mechanical ventilation via a tracheostomy. Magnetic resonance imaging subsequently suggested an intramedullary tumour from C₇ to the medulla and possibly the pons (Fig. 2).

Her lungs were still ventilated via the tracheostomy 6 months later but she was unresponsive and quadriplegic.



Fig. 2. Magnetic resonance image of patient 5 showing high cervical cord and brain stem tumour (arrowed) which appears white.

Table 1. Patient characteristics.

Case no.	Age (years)	Pathology	Duration of operation (hours)	Sitting	Time of postoperative onset (hours)	Treatment and outcome
1	27	Bilateral acoustic neuroma	14	No	8	Tracheostomy, resolved 14 days
2	32	Acoustic neuroma	12	No	8	Tracheostomy, resolved 14 days
3	54	Meningioma	8	No	36	Conservative, resolved 5 days
4	24	Acoustic neuroma	12	No	0	Tracheostomy, resolved 13 days
5	48	Intramedullary astrocytoma	—	—	see text	Died (unrelated)
6 ¹	2	Cerebellar mass	6	Yes	0	Tracheostomy, died 4 days
7 ¹	45	?	10	Yes	0	Resolved 1 day
8 ²	21	Arteriovenous malformation	14	Yes + induced hypotension	0-4	Tracheostomy, resolved 21 days
9 ³	30	Arteriovenous malformation	12	Yes	0-2	Intubated 17 days, died 22 days (unrelated)
10 ^{4,5}	1.5	Stenotic foramen magnum (achondroplasia)	5	Yes	0	Tracheostomy, resolved 3 months

She spontaneously developed marked swelling of the tongue which protruded 2 cm from the mouth after a week. Despite conservative measures it remained swollen until her death a week later.

Neuropathological examination revealed an anaplastic astrocytoma of the upper spinal cord. There was expansion of the tegmentum of the mid-brain and pons and the whole medulla was enlarged, although tumour infiltration and necrosis were present only in the lower half of the medulla. In addition, the cerebral hemispheres showed evidence of 'watershed' infarcts in the boundary zone between the distribution of the anterior and middle cerebral cortices bilaterally; these were many weeks old.

Discussion

Acute macroglossia was reported in 1974 in two patients as a rare sequel to neurosurgery in the sitting position. There have since been four further case reports²⁻⁵ and in each the sitting position was implicated (Table 1). However, two of these reports^{4,5} almost certainly describe the same patient and we have considered them as one. The authors considered that macroglossia was secondary to venous obstruction and thrombosis of the lingual or even internal jugular veins bilaterally. Marked flexion of the neck, pressure of the tracheal tube and possibly induced hypotension were blamed. One case of hemimacroglossia was described after neurosurgery in the supine position but there was probably local trauma to the tongue.⁶ The authors also postulated venous congestion but this is unlikely since bilateral swelling would probably have resulted. Trauma can cause macroglossia, as shown by a case in which swelling developed after epileptic tongue biting unrelated to neurosurgery.⁷

A recent textbook⁸ suggests that macroglossia is a hazard of the semi-sitting position and is due to protrusion of the tongue through the teeth or against a hard airway. It is claimed that the complication can be prevented by careful attention to positioning pre-operatively. Other recommendations have included the use of a bite block and avoidance

of an oral airway and of extreme neck flexion. Hourly visual checking of the tongue, head and neck has also been suggested, with repositioning if any evidence of venous obstruction is seen.⁶ However, this is not feasible in our own practice since access to the head is severely restricted once surgery commences.

The sitting position was not used but our fourth case otherwise closely resembles those described in the literature in that there was marked neck flexion and evidence of intra-operative venous congestion, and macroglossia occurred immediately. The other cases, however, do not fall into this category. The sitting position was not used and these patients did not have extreme neck flexion, an oral airway or induced hypotension. The onset of macroglossia was delayed. The fifth patient did not undergo surgery. She already had a long-standing tracheostomy when macroglossia developed so pressure on the lingual and neck veins was unlikely, as was marked neck flexion.

We reviewed our records for the period December 1980-July 1986, during which 320 posterior fossa craniectomies were performed and the first three cases of macroglossia occurred, which gives an incidence of 1%. The sitting position was used in 83 patients (26%) but none of these developed macroglossia. The mean duration of posterior fossa surgery over this period was 6 hours 20 minutes (range 2-18 hours). Macroglossia developed only after prolonged operations (14, 12, 8 and 12 hours), as in previous reports.

We propose that just as pulmonary oedema can have a neurogenic origin,⁹ macroglossia can be caused by abnormal brain stem discharges. Abnormal impulses may be provoked by surgical manipulation or tumour infiltration. In support of this theory, our four surgical patients had large, technically difficult lesions that required prolonged dissection around the brain stem. Macroglossia has not been reported to follow supratentorial neurosurgery, despite equally long operations, which suggests that the relevant stimulus is specific to the posterior fossa. Our fifth patient developed macroglossia as the tumour extended cranially, just as it was beginning to involve the nuclei

of the lower cranial nerves but before it destroyed them completely.

Neurogenic pulmonary oedema may occur with hind-brain lesions or after head injury or neurosurgery. The mechanism has not been elucidated fully but profound sympathetic activity has been implicated. The injection of a fibrin-forming mixture into the basal cistern in animal experiments produces severe pulmonary oedema and this response is blocked by vagotomy. It seems that the permeability of the lung capillaries is affected by an outflow of stimuli from the brain stem via the vagus nerves.⁹ The brain stem is intimately involved with the autonomic supply to the tongue, pharynx and lower face, and similar mechanisms may be involved in the production of macroglossia.

There are several practical points to make whichever theory is correct (and they are not mutually exclusive). Postoperative macroglossia is not confined to operations in the sitting position although it does seem to occur only after posterior fossa surgery. It tends to follow the more lengthy procedures and its onset may be delayed for many hours. Re-intubation may be difficult or impossible once the swelling is established, and emergency tracheostomy may be required. The swelling resolves spontaneously but this may take up to 2 weeks and it seems sensible in the meantime to use bite blocks to prevent damage from the teeth and to facilitate oral toilet. Pain in the tongue was a prominent feature in every case even before trauma had occurred from pressure of the teeth. Systemic and topical analgesics were required; in this respect we found topical lignocaine of more value than benzydamine hydrochloride oral rinse.

Macroglossia might still be caused by local trauma or venous obstruction. The risks would be minimised by the use of a nasotracheal tube intra-operatively in addition to the precautions mentioned above. A nasal tube is less likely to do further damage if swelling develops and is also more comfortable.

Full-blown macroglossia is a dramatic, unmistakable and potentially fatal problem which is not likely to be under-reported. It is interesting that our cases all occurred within the last seven years and it is only 13 years since the first case was reported in the literature. Our neuroanaesthetic

colleagues, including retired members of the department, do not recall any previous cases. Could it be that this is truly a new complication and, if so, is it related to changes in neuroanaesthetic or neurosurgical practice? For instance, new techniques allow tumour resection with much less local destruction of tissue, so that adjacent normal structures may be irritated rather than ablated.

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References

1. McALLISTER RG. Macroglossia—a positional complication. *Anesthesiology* 1974; **40**: 199–200.
2. ELLIS SC, BRYAN-BROWN CW, HYDERALLY H. Massive swelling of the head and neck. *Anesthesiology* 1975; **42**: 102–3.
3. TATTERSALL MP. Massive swelling of the face and tongue. *Anaesthesia* 1984; **39**: 1015–7.
4. MAYHEW JF, MINER M, KATZ J. Macroglossia in a 16 months old child after a craniotomy. *Anesthesiology* 1985; **62**: 683–4.
5. DENNENY JC III. Postoperative macroglossia causing airway obstruction. *International Journal of Pediatric Otorhinolaryngology* 1985; **9**: 189–94.
6. TEEPLE E, MAROON J, RUEGER R. Hemimacroglossia and unilateral ischemic necrosis of the tongue in a long-duration neurosurgical procedure. *Anesthesiology* 1986; **64**: 845–6.
7. HOLMES W, BALI IM. A case of acute macroglossia. *Today's Anaesthetist* 1986; **1**: 26–7.
8. RUBIN RC, FROST EAM. Posterior cranial fossa surgery. In: FROST EAM, ed. *Clinical anesthesia in neurosurgery*. Boston: Butterworth, 1984: 161, 181–2.
9. WALTER JB, ISRAEL MS. *General pathology*, 5th edn. Edinburgh: Churchill-Livingstone, 1979: 527.

CASE REPORT

Malignant hyperthermia in the Wolf–Hirschhorn syndrome

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Summary

A case of malignant hyperthermia in a small child with a chromosomal abnormality is described. The management of malignant hyperthermia in very small children is discussed.

Key words

Complications; Wolf-Hirschhorn syndrome.

Hyperthermia; malignant.

The Wolf–Hirschhorn syndrome is a rare chromosomal abnormality in which there is deletion of the short arm of chromosome no. 4. Features of the condition include poor intra-uterine growth, severe psychomotor retardation, characteristic facies and various congenital midline fusion anomalies. These include cleft lip or palate, ventricular or atrial septal defects, hypospadias and midline scalp defects.¹ Epileptic seizures are common, as are eye and renal abnormalities.² Prognosis is poor: 34% of children die by the age of 2 years, either of cardiac failure or bronchopneumonia.

The combination of these abnormalities may present a considerable anaesthetic challenge. We present the case of a small infant with this rare syndrome, which was further complicated by an episode of malignant hyperthermia.

Case history

A 21-month-old female, weight 5.2 kg, was admitted for repair of cleft palate. She was below the tenth centile for both height and weight and was known to have Wolf–Hirschhorn syndrome. She was microcephalic, hypotonic, unable to sit unaided and suffered from epilepsy and recurrent respiratory tract infection associated with feed aspiration. Palatal repair was attempted in order to reduce the number of hospitalisations for chest infection and to obviate the frequent need for naso-enteral feeding. There were two older siblings, both normal, aged 2 and 4 years. The family had no history of neuromuscular disease or anaesthetic mishap.

She underwent vigorous chest physiotherapy for one

week prior to surgery. Premedication was with intramuscular atropine 0.2 mg and anaesthesia was induced with 50% cyclopropane in oxygen. The agents were changed after induction, to halothane 2% in oxygen at 6 litres/minute. Suxamethonium 10 mg was then given intravenously through a small vein on the palmar aspect of the right wrist. Tracheal intubation was difficult because of poor visualisation of the glottis and was eventually achieved with a 3.5 mm child's anatomical (CAT) tube while she breathed spontaneously 4% halothane in oxygen. Venous cannulation also proved to be difficult and was accomplished with a cannula in the right external jugular vein.

The halothane concentration was reduced to 0.5% and tubocurarine 2 mg was given 50 minutes after induction. The child was moved into the operating theatre 5 minutes later and placed on an air-driven warming mattress.³ Her lungs were ventilated with a T-piece breathing system with a Penlon Series 200 ventilator and a Newton paediatric valve. Monitoring consisted of electrocardiogram, automated sphygmomanometer (Dinamap, Critikon Ltd), precordial stethoscope, rectal temperature probe (Ellab) and a ventilator cycling alarm (BOC Medishield).

Seventy minutes after induction of anaesthesia she was noted to be moving and to have a rectal temperature of 38.5°C. The warming mattress was switched off and a second dose of tubocurarine 2 mg given. The temperature increased over the next 10 minutes to 42.2°C and spontaneous ankle clonus developed.

Surgery was discontinued and the child's lungs hand-ventilated with 100% oxygen from a cylinder using a fresh T-piece. Dantrolene 1 mg/kg, hydrocortisone 25 mg and

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Table 1. Arterial blood gas estimations.

Time* (minutes)	pH	P _{CO} ₂ (kPa)	P _O ₂ (kPa)	Standard bicarbonate (mmol/ litre)	Base excess (mmol/ litre)	F _{IO} ₂
85	7.37	3.77	54.32	16.2	- 7.8	1.0
135	6.96	11.77	18.57	18.7	- 13.8	1.0
185	7.12	7.60	42.23	17.7	- 11.6	1.0
225	6.89	11.46	18.19	15.4	- 15.9	1.0
300	6.98	8.83	24.04	14.5	- 15.5	1.0
345	7.18	8.41	20.44	15.4	- 12.3	1.0
390	7.31	3.40	34.93	12.6	- 12.1	0.3

* From induction.

frusemide 3 mg were given intravenously. The infusion was changed to cold plasma protein fraction and a femoral arterial blood sample was taken for blood gas estimation (Table 1). She was cold sponged while a cannula was inserted in the left radial artery for direct arterial pressure monitoring.

The temperature decreased to 38.5°C at 90 minutes but then increased again rapidly to 39.5°C. Ice became available and was packed in the groin and axillae. The patient was transferred to the intensive care unit and paralysed with pancuronium to facilitate ventilation. Considerable difficulty was nevertheless experienced in maintaining normocarbida. The ventilator used was a Siemens Servo 900C. Further doses of dantrolene 1 mg/kg were given half-hourly to a total dose of 7 mg/kg (105 ml at the recommended dilution) before the pyrexia abated. Bladder irrigation with cold saline at 4°C was performed to aid cooling. It took 5 hours from the initial temperature rise for the child to become afebrile.

Results of blood gas analyses are shown in Table 1. Metabolic acidosis was treated with intravenous sodium bicarbonate 8.4%. The child's lungs were ventilated overnight. The trachea was extubated the following day without problem and apart from an intercurrent chest infection, she subsequently regained her normal state of health.

Discussion

Malignant hyperthermia is a feared complication of general anaesthesia with a probable overall incidence of 1:40 000.⁴ Delay in diagnosis increases the chances of a fatal outcome so successful management requires clinical alertness and prompt treatment.⁵ Prior recognition of individuals who might be at risk would increase the safety of general anaesthesia for these patients.

No reliable noninvasive test is available for the determination of a patient's susceptibility to the disease.⁴ Recognition of the child who is potentially susceptible to malignant hyperthermia relies at present, either upon the elucidation of a positive past or family history, or upon the possible association between certain medical conditions and malignant hyperthermia. *In vitro* screening of muscle biopsy specimens⁶ is unreliable in children under the age of 10 years.⁷

Some forms of the condition appear to be inherited primarily as an autosomal dominant⁸ but inheritance is likely to be multifactorial,^{5,9} with variable susceptibility to trigger agents. Malignant hyperthermia can be associated with a myopathy in its own right, or with the myopathy of another medical condition which may itself be inherited, for example the myopathy of osteogenesis imperfecta.⁴

This case report appears to be the first in which malignant hyperthermia has been seen in association with the Wolf-Hirschhorn syndrome. A review of the records of the three other patients with the syndrome who have attended this hospital, showed that only one of these patients underwent general anaesthesia and this was uneventful. There are no reports in the literature of anaesthetic problems in these children. Furthermore, no case reports were found of malignant hyperthermia in patients with any other chromosomal abnormality.

Episodes of malignant hyperthermia in infants and young children are increasingly recognised. Pollock and Britt¹⁰ in a review of 734 crises showed that 280 of these occurred during anaesthesia for head and neck surgery. The crises were most frequent in the child, adolescent and young adult, and the largest number of reactions occurred during tonsillectomy, adenoidectomy or grommet insertion. Facial plastic cases accounted for the next largest group. Cases of suspected malignant hyperthermia have been reported in a 6-month-old¹¹ and a 14-month-old child.¹²

Two points of interest arise from this case. Firstly, the weight of the 6-month-old child mentioned above, the smallest reported in the literature to date, was 7 kg. The weight of our patient was 5.2 kg. The recommended practice of infusing quantities of cold intravenous fluid to assist cooling, may be impractical in these small subjects because of the danger of volume overload. Indeed, in our patient the total volume administered of dantrolene alone (105 ml) represented an appreciable proportion of the calculated blood volume (25%). Irrigation of the bladder with cold sterile saline to aid cooling, proved very effective in this situation. Furthermore, this technique may be safer than gastric irrigation for cooling, since it avoids the potential hazard of airway soiling.

Secondly, chromosomal deletion syndromes may be of use in gene mapping.¹³ Further reports of malignant hyperthermia in patients with the Wolf-Hirschhorn syndrome or any other chromosomal abnormality may help in the elucidation of the pathogenesis of the condition.

The association between malignant hyperthermia and the Wolf-Hirschhorn syndrome is as yet unproven. We advise, nevertheless, that temperature should be monitored and every care taken to see that appropriate facilities for the treatment of malignant hyperthermia are readily to hand if any patient with this condition is to be anaesthetised.

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References

- JOHNSON VP, MULDER RD, HOSEN R. The Wolf-Hirschhorn (4p-) syndrome. *Clinical Genetics* 1976; **10**: 104-12.
- LAZJUK GI, LURIE IW, OSTROWSKAJA TI, KIRILLOVA IA, NEDZVED MK, CHERSTVOY ED, SILYAEVA NF. The Wolf-Hirschhorn syndrome. Part II. Pathologic anatomy. *Clinical Genetics* 1980; **18**: 6-12.
- NIGHTINGALE P, MEAKIN G. A new method for maintaining body temperature in children. *Anesthesiology* 1986; **65**: 447-8.
- ELLIS FR, HEFFRON JJA. Clinical and biochemical aspects of malignant hyperpyrexia. In: ATKINSON RS, ADAMS AP, eds. *Recent advances in anaesthesia and analgesia*, Vol. 15. Edinburgh: Churchill Livingstone, 1984: 173-207.

5. GRONERT GA. Malignant hyperthermia. *Anesthesiology* 1980; **53**: 395-423.
6. ELLIS FR, HALSALL PJ, ORDING H, FLETCHER R, RANKLEY E, HEFFRON JJA, LEHANE M, MORTIER W, STEINBEREITNER K, SPORN P, THEUNYNCK D, VERBURG R. A protocol for the investigation of malignant hyperpyrexia (MH) susceptibility. *British Journal of Anaesthesia* 1984; **56**: 1267-9.
7. ELLIS FR. Malignant hyperpyrexia. *Archives of Disease in Childhood* 1984; **59**: 1013-15.
8. BRITT BA, LOCHER WG, KALOW W. Hereditary aspects of malignant hyperthermia. *Canadian Anaesthetists' Society Journal* 1969; **16**: 89-98.
9. ELLIS FR, CAIN PA, HARRIMAN DGF. Multifactorial inheritance of malignant hyperpyrexia susceptibility (MHS). *British Journal of Anaesthesia* 1977; **49**: 514-5.
10. POLLOCK RA, BRITT BA. Malignant hyperthermia in the head and neck surgery patient: an update and review. *Laryngoscope* 1983; **93**: 318-25.
11. FAUST DK, GERGIS SD, SOKOLL MD. Management of suspected malignant hyperpyrexia in an infant. *Anesthesia and Analgesia* 1979; **58**: 33-5.
12. HENSCHEL EO, KAH TB. Malignant hyperthermia in a 14-month old infant. In: HENSCHEL EO, ed. *Malignant hyperthermia: current concepts*. New York: Appleton-Century Crofts, 1977: 57-61.
13. GUSELLA JF, TANZI RE, BADER PI, PHELAN MC, STEVENSON R, HAYDEN MR, HOFMAN KJ, FARYNIARZ AG, GIBBONS K. Deletion of Huntington's disease-linked G8 (D4S10) locus in Wolf-Hirschhorn syndrome. *Nature* 1985; **318**: 75-8.

CASE REPORT

Myoclonic spasms following intrathecal morphine

M. J. GLAVINA AND R. ROBERTSHAW

Summary

Myoclonic twitching in the lower limbs of a patient who received intrathecal narcotics is described. There was no loss of consciousness. Reports of this phenomenon in animals are reviewed.

Key words

Analgesics, narcotic; morphine.

Complications; myoclonus

Intrathecal morphine has been used increasingly over the past few years and consistently produces prolonged and intense analgesia.^{1,2} It is particularly effective in the treatment of intractable pain in patients with disseminated malignancy and in whom life expectancy is short. The complication most usually associated with this form of administration, respiratory depression, is rarely encountered in this group of patients who are often prescribed large doses of narcotic analgesics for long periods.

We report here a patient who developed myoclonic spasms of the legs whilst she received treatment with intrathecal morphine.

Case history

A 59-year-old woman presented with intractable pain in the leg, caused by infiltration of secondary adenocarcinoma into the body of the L₅ vertebra. A primary carcinoma of colon had been resected 2 years previously. There was no previous history of epilepsy or other neurological disease. Radiotherapy and a cervical cordotomy effectively eliminated pain in one leg but severe pain in the low back, sacrum and other leg persisted. Background analgesia was provided with oral sustained-release morphine sulphate tablets, 60 mg 6-hourly and indomethacin.

A narrow-bore plastic catheter was inserted into the subarachnoid space, its position confirmed by aspiration of cerebrospinal fluid (CSF) and an intrathecal infusion of morphine sulphate commenced at a rate of 160 µg/hour. The preparation contained 0.1% w/v sodium metabisulphite as preservative (Macarthy Ltd, Romford, Essex). This small quantity was then diluted to a convenient volume in saline for infusion using an electrically-driven syringe pump.

Pain relief was improved for the first 36 hours after the infusion was started; however, symptoms returned over the next 5 days so the infusion rate was increased in stages to 1250 µg/hour by the fifth day, with some improvement in pain control. A bolus of morphine was given intrathecally at this stage when the syringe was changed, amounting to approximately 3000 µg. The patient developed sudden episodic myoclonic spasms of the lower limbs within 40 minutes. Each spasm lasted 5–10 seconds and spasms occurred at 30–40-second intervals. All muscle groups in the upper legs were affected symmetrically and there were concurrent spasms of the lower abdominal muscles. The resultant intermittent posturing was a combination of extension and abduction at the hips. These spasms caused the patient distress and exacerbated her symptoms of pain in the lower limbs and back. There was no evidence of cerebral epileptic activity or of respiratory depression, and no reduction in the patient's conscious level. She remained lucid and aware throughout. Two doses of intravenous diazepam 10 mg failed to prevent the spasms.

Eventually, 3 ml of plain 0.5% bupivacaine was injected after careful aspiration of the catheter deadspace. This completely abolished the spasms and resulted in a sensory level to T₇. The catheter was then removed.

Neurological examination after the effects of the local anaesthetic had worn off did not reveal any abnormality attributable to the procedure; however, in spite of this, the patient still complained of the unpleasant sensation of continued muscle spasms for 24 hours. There were no late complications.

Discussion

The term 'myoclonus' is applied to brief, shock-like muscular contractions which may involve a whole muscle or may

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rarely be limited to a small number of muscle fibres. Contractions often occur symmetrically in muscle groups on opposite sides of the body.³ The intraspinal administration of morphine was first described to cause twitching and tremor in dogs in 1915.⁴ Myoclonic twitches have been observed to follow the injection of intrathecal morphine in rats and this action resembles the human syndrome of action myoclonus.⁵ Intrathecal morphine in high dosage in the rat causes alternating clonic contractions of the hind-paws, often preceded by a tonic extension of these limbs.⁶ Significantly, animals made tolerant to the analgesic effects of morphine display potentiated convulsant activity of the hindlimbs following intrathecal morphine. There is also indirect evidence that the convulsant action of morphine, when given systemically in high doses, is mediated in part at the level of the spinal cord.⁷ However, it is not clear whether the action of intrathecal morphine is related to an effect on specific opiate receptors at the level of the spinal cord only.⁸

Some of these anomalies are probably explained by the wide variation in morphine doses administered and by differences in response to opiates among various species. A search of the literature did not reveal any reports of this complication in man. However, an apparent seizure in which the patient lost consciousness was reported following inadvertent intrathecal morphine.⁹

The possibility that the myoclonus seen in this case was a toxic effect of the preservative compound, was considered. Previously paralysis has been described^{10,11} when neurological side effects have been caused by preservatives in solutions applied intrathecally and epidurally. The preservative contained in our preparation of morphine was 0.1% sodium metabisulphite which has not been reported to cause neurological complications; indeed, the substances which have been implicated are organic chemical com-

pounds, namely benzyl alcohol and methyl hydroxybenzoate.

Our patient received high doses of intrathecal morphine and undoubtedly exhibited tolerance to the analgesic action of opioid drugs: she required large doses of oral morphine sulphate to control her pain for some weeks prior to hospital admission. It is of further interest that the bolus of drug administered did not relieve the pain caused to the patient by the myoclonus.

References

1. WALTON JN. *Brains' diseases of the nervous system*, 8th edn. Oxford: Oxford Medical Publications, 1984.
2. COUSINS MJ, MATHER LE, GLYNN CJ, WILSON PR, GRAHAM JR. Selective spinal analgesia. *Lancet* 1979; **1**: 1141-2.
3. SAMII K, FERET J, HARARI A, VIARS P. Selective spinal analgesia. *Lancet* 1979; **1**: 1142.
4. MCGUIGAN H, ROSS EL. Intraspinal administration of morphine. *Journal of the American Medical Association* 1915; **64**: 1494.
5. SHOHAMI E, EVRON S. Intrathecal morphine induces myoclonic seizures in the rat. *Acta Pharmacologica et Toxicologica* 1985; **56**: 50-4.
6. FRENK H, WATKINS LR, MEYER DJ. Differential behavioral effects induced by intrathecal microinjection of opiates. Comparison of convulsive and cataleptic effects produced by morphine, methadone, and D-alà 2-methionine ekephalinamide. *Brain Research* 1984; **299**: 31-42.
7. DIB B. A study of intrathecal self-injection of morphine by rats, and the difficulties entailed. *Pain* 1985; **23**: 177-85.
8. FRENK H, LIBAN A, BALAMUTH R, URCA G. Opiate and non-opiate aspects of morphine induced seizures. *Brain Research* 1982; **253**: 253-61.
9. LANDOW L. An apparent seizure following inadvertent intrathecal morphine. *Anesthesiology* 1985; **62**: 545-6.
10. GAGLIANO RG, COSTANZI JJ. Paraplegia following intrathecal methotrexate. *Cancer* 1976; **37**: 1663-8.
11. CRAIG DB, HABIB GG. Flaccid paralysis following obstetrical epidural anaesthesia; possible role of benzoyl alcohol. *Anesthesia and Analgesia* 1977; **2**: 219-22.

CASE REPORT

A severe coagulopathy following volume replacement with hydroxyethyl starch in a Jehovah's Witness

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Summary

Blood volume was maintained by an infusion of hydroxyethyl starch 2000 ml (Hespan: HES) during and for the first 28 hours after a major orthopaedic operation in a 13-year-old girl who was a Jehovah's Witness. This was responsible for a generalised clinical haemorrhagic state, an acquired coagulopathy associated with a shortened thrombin, prolonged prothrombin and activated partial thromboplastin times, and an acquired von Willebrand syndrome. The coagulation, after cessation of the infusion of HES, did not become normal until approximately 72 hours later.

Key words

*Complications; acquired coagulopathy.
Organisations; Jehovah's Witnesses.*

Blood volume is routinely maintained by infusions of human red cell products, synthetic colloid solutions and human albumin fractions after major operative procedures. Jehovah's Witnesses, because of their religious beliefs, do not allow the transfusion of any human red cell or plasma product even in situations which threaten life.¹ Blood and fluid loss has to be minimised and replaced by crystalloid and synthetic colloid infusions alone to maintain a satisfactory blood volume and prevent hypovolaemic shock, if major surgery is to be undertaken in these patients.^{2,3}

Hydroxyethyl starch (HES) is a synthetic macromolecule prepared from the waxy species of amylopectin in maize and is available as a 6% solution with a molecular weight average of 450 000 as a volume expander.⁴ Volume augmentation approximately equals the volume infused but because it retains 30–35% of this effect 24 hours later it is ideal as a volume expander after trauma or operative procedures. Previous studies have shown that infusions of HES of between 0.5–1.4 g/kg, during the peri-operative and first 24-hour postoperative period after major orthopaedic operations, were a safe and effective means of volume expansion.^{5,6} In view of this experience it was planned to maintain blood volume in a patient who was a Jehovah's Witness with HES during and following a major orthopaedic spinal operation.

Case history

A 13-year-old Caucasian schoolgirl who weighed 45 kg with a 2-year history of backache was referred for an ortho-

paedic opinion after a right-sided thoracic curve was noted at a school medical examination. She was a fit girl with no history of easy bruising or a prolonged bleeding tendency. There was no family history of a bleeding diatheses or scoliosis. On examination she had a right lower thoracic scoliosis. Forward flexion revealed a rib hump and a small left lumbar hump. Spinal X rays showed curvature of T₅–T₁₂ with a thoracic lordosis on lateral views. A diagnosis of idiopathic adolescent scoliosis was made and surgical correction with stabilisation of this curve was recommended.

Her parents are Jehovah's Witnesses and whilst they wanted surgical correction to be performed they were not prepared to accept blood transfusion in any form. This also excluded peri-operative venesection and replacement at the end of the procedure, autologous transfusion, or the use of human plasma products such as fresh frozen plasma and cryoprecipitate.

Pre-operative investigations showed a normal full blood count (Hb 14.5 g/dl, platelets 355×10^9 /litre), normal biochemistry screen and a mild restrictive defect on pulmonary function testing.

A posterior spinal fusion with Harrington–Luque instrumentation was carried out and planned profound hypotension was maintained throughout the operation. Blood volume throughout the 3.5 hours of the operation was maintained by a continuous infusion of hydroxyethyl starch (HES 450 000/0.7; Hespan 6.0 g/100 ml). Total blood loss was estimated at 500 ml, and 1000 ml of HES was infused during the operation.

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Table 1. Haemostatic parameters postoperatively. The infusion of HES was stopped 28 hours postoperatively. The units and normal range is shown for each of the parameters measured.

Hours after operation	Hb (11-17) g/dlitre	Platelets (150-400) × 10 ⁹ /litre	Thrombin time (12-14) seconds	Prothrombin time (13-17) seconds	APTT (30-40) seconds	Fibrinogen (1.5-4.0) g/litre	Factor X (0.5-2.0) u/ml	Factor VII (0.5-2.0) u/ml	Factor VIII:C (0.5-2.0) u/ml	vWF (0.5-2.0) u/ml	vWFag (0.5-2.0) u/ml
26	6.6	251	11	32	90	1.7	0.36	0.06	0.17	0.08	0.18
30	6.7	286	9	39	71	2.1	—	0.11	0.40	0.23	0.36
40	6.5	315	10	32	56	3.8	0.54	0.11	0.98	0.30	0.66
52	6.0	335	—	30	—	3.3	0.68	0.11	0.72	0.56	0.82
68	6.2	329	13	20	42	3.1	0.81	0.15	1.70	1.10	1.16
92	8.1	751	14	17	38	3.1	—	0.39	—	—	—

vWF = von Willebrand factor.
vWFag = von Willebrand antigen.

Postoperatively in the intensive care unit for the first 28 hours blood volume was maintained by a further 1000 ml infusion of HES. The patient had a persistent sinus tachycardia of approximately 120/minute but maintained an adequate cardiac output and blood pressure during this period.

Twenty-six hours postoperatively continual brisk blood loss was observed to have occurred from the site of the surgical incision which was not controlled by local pressure. Laboratory investigation then revealed Hb 6.6 g/dl, platelets 251 × 10⁹/litre, thrombin time 11 seconds (control 12 seconds) prothrombin time (PT) 32 seconds, (control 15 seconds) and activated partial thromboplastin time (APTT) 90 seconds (control 40 seconds). The HES infusion was stopped in view of the bleeding diathesis, and subsequently blood volume maintained with crystalloids alone. Despite repeated pleas to the parents permission was refused to transfuse any red cell or plasma products. The results of more detailed and subsequent haemostatic investigations are shown in Table 1.

Blood loss from the incision gradually decreased over the next 20 hours and eventually ceased. This corresponded to a shortening of the prolonged prothrombin time and APTT, but they did not become completely normal until 92 hours postoperatively.

Subsequent coagulation factor assays showed a shortened thrombin time compared with the control times, a high normal fibrinogen level, an acquired von Willebrand's syndrome with markedly reduced levels of factor VIII:C and von Willebrand's factor (vWF) and reduced levels of factors VII and X. These defects were maximal when the first postoperative sample was taken (26 hours postoperatively) and corrected gradually after stopping the HES infusion (Table 1).

Discussion

Hypovolaemia with consequent underperfusion of vital organs is a hazard of major surgical procedures.⁷ Restoration and maintenance of an adequate blood volume is controlled increasingly with colloids, such as dextran and hydroxyethyl starch.⁸ These synthetic colloids have a macromolecular structure that ensures preferential retention in the blood stream (unlike crystalloids) and which augment blood volume and maintain oncotic pressure. They have been used successfully in Jehovah's Witnesses who undergo surgery, and even enable cardiac bypass procedures to be performed.

The haemodynamic benefits of HES are quite clear^{4,8} but their effects on haemostasis are controversial. No episodes of clinical bleeding were reported in the four studies^{5,6,9,10} in which HES was used in the management of acute hypovolaemia. Three of these studies reported mild elevations of the PT and APTT in recipients of HES. The mean volumes of HES given to each patient ranged from 835 to 3600 ml.

There are three mechanisms by which synthetic macromolecular colloids have been reported to cause haemostatic defects.⁵ Firstly, the thrombin time is shortened by a fibrinoplastic effect of the macromolecules in HES. This accelerates the conversion of fibrinogen to fibrin but causes a less stable thrombus which is much more readily susceptible to lysis. Secondly, the macromolecules induce an acquired von Willebrand's syndrome with reduced levels of

all three main factor VIII parameters, factor VIII:C, vWF and von Willebrand factor antigen (vWFag). This was most marked with vWF activity and levels of 0.08 iu/ml (normal range 0.5–2.0 iu/ml) with associated reduced levels of VIII:C occurred and were probably primarily responsible for the excessive postoperative bleeding. Thirdly, macromolecules may coat the outer membrane of circulating platelets and cause a qualitative platelet function defect and prolong the bleeding time. Minor degrees of platelet aggregation abnormalities have been previously observed after infusion of lower volumes of HES and it is probable that platelet defects were contributory to the haemorrhagic state. Unfortunately, platelet function tests, which have to be performed on fresh blood samples, were not investigated in this emergency situation. The bleeding diathesis was worsened by a dilutional effect caused by subsequent crystalloid infusion and enhanced coagulation factor consumption. This was most marked by reduced factor VII activity to 0.06 iu/ml which has the shortest half life, of approximately 4 hours, of all the coagulation factor proteins.

In patients who are not Jehovah's Witnesses these defects would have been readily corrected by an infusion of red cells, fresh frozen plasma, cryoprecipitate and platelet concentrates. However, in this patient the prolonged half life of 25.5 hours of HES delayed the correction of the haemostatic defect and effective clinical haemostasis did not occur until 24 hours after stopping the infusion. This patient received 2000 ml of HES equivalent to 2.66 g/kg and a replacement of approximately 60% of her total blood volume. Previous clinical studies with infusions of HES up to 1.4 g/kg have not caused clinical bleeding episodes although minor laboratory defects of a similar nature have been reported. This case report highlights the potential haemorrhagic problems that may develop acutely when

blood volume is maintained by a massive infusion of macromolecules such as HES when given as the sole fluid to prevent hypovolaemia.

Acknowledgment

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References

1. SACKS DA, KOPPEL RH. Blood transfusion and Jehovah's Witnesses: medical and legal issues of obstetrics and gynecology. *American Journal of Obstetrics and Gynecology* 1986; **154**: 483–6.
2. CLARKE JFM. Surgery in Jehovah's Witnesses. *British Journal of Hospital Medicine* 1982; **27**: 497–500.
3. HENDERSON AM, MARYNIAK JK, SIMPSON JC. Cardiac surgery in Jehovah's Witnesses. A review of 36 cases. *Anaesthesia* 1986; **41**: 748–53.
4. MISHLER JM. *Pharmacology of hydroxyethyl starch. Use in therapy and blood banking*. New York and Oxford: Oxford University Press, 1982.
5. MACINTYRE E, MACKIE IJ, HO D, TINKER J, BULLEN C, MACHIN SJ. The haemostatic effects of hydroxyethyl starch (HES) used as a volume expander. *Intensive Care Medicine* 1985; **11**: 300–3.
6. SHATNEY CH, DEEPIKA K, MILITELLO PR, MARJERUS TC, DAWSON RB. Efficacy of hetastarch in the resuscitation of patients with multisystem trauma and shock. *Archives of Surgery* 1983; **118**: 804–9.
7. MACINTYRE E, BULLEN C, MACHIN SJ. Fluid replacement in hypovolaemia. *Intensive Care Medicine* 1985; **11**: 231–3.
8. MISHLER JM. Synthetic plasma volume expanders—their pharmacology, safety and clinical efficacy. *Clinics in Haematology* 1984; **13**: 75–92.
9. DIEHL JT, LESTER JL 3rd, COSGROVE DM. Clinical comparison of hetastarch and albumin in postoperative cardiac patients. *Annals of Thoracic Surgery* 1982; **34**: 674–9.
10. PURI VK, PAIDIPATY B, WHITE L. Hydroxyethyl starch for resuscitation of patients with hypovolemia and shock. *Critical Care Medicine* 1981; **9**: 833–7.

Anaesthesia for carbon dioxide laser laryngeal surgery in infants

A new tracheal tube

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Summary

Problems associated with the presence of a tracheal tube during anaesthesia for infant laryngeal surgery using the carbon dioxide laser are described. This paper discusses alternatives and describes an effective anaesthetic technique and a new tracheal tube.

Key words

Equipment; tubes, tracheal.

Surgery; laryngeal.

The carbon dioxide laser has been in surgical use for about 15 years. It is well known that a considerable fire hazard is associated with the tracheal tube and sequelae range from minor tissue damage to intra-operative death.^{1–3}

A variety of methods have been advocated to reduce or remove this hazard. The tracheal tube may be protected either with aluminium foil wrapped around the tube^{4,5} or by suitably positioned water-soaked swabs.^{4–6} A Venturi technique⁷ may be used, or the tracheal tube may be replaced by a nonflammable alternative.^{8,9} The hazard can also be lessened by reduction of the oxygen concentration, by the intermittent use of air whilst laser surgery is in progress.¹⁰

Plastic materials, such as tracheal tubes, nasogastric and tracheostomy tubes, must never be used in a patient who undergoes carbon dioxide laser surgery.⁸ A foil-wrapped red rubber tracheal tube can be used but wrapping of a small tube is technically difficult. It is much more likely to be traumatic and more liable to kink than an adult foil-wrapped tube. Spiral wrapping of the tube makes it rigid, while kinking is even more likely if the tape is applied longitudinally. Airways obstruction caused by pieces of tape breaking off has been reported.¹¹ It is possible to protect an adult tracheal tube with soaked swabs but the reduction of surgical access makes this technique impossible in children. The use of a totally fireproof metal tube was first suggested by Norton.⁹ A range of flexible metal tubes is available in this country. The smallest tube in the range has a diameter of 5 mm, and is suitable for larger children; however, a modification has been designed for smaller children and incorporates both a rigid with a flexible portion (Fig. 1). The Oswal–Hunton paediatric metal

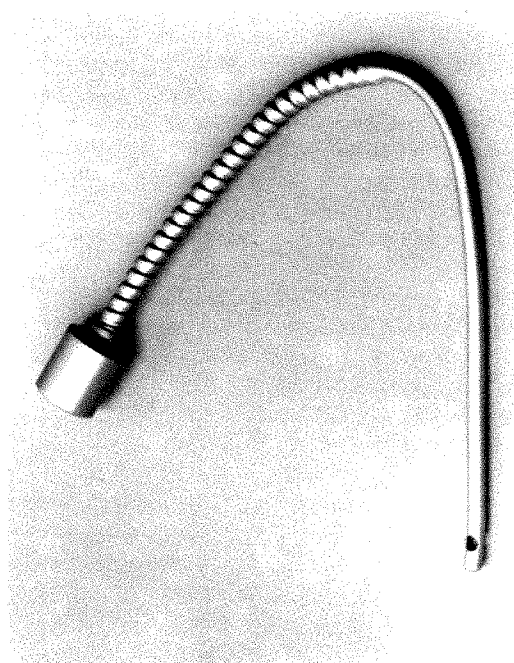


Fig. 1. The Oswal–Hunton paediatric metal tracheal tube.

tracheal tube is manufactured in several lengths* and was designed from experience with infants (less than one year old). Radiography was used to determine the optimum shape. The rigid part allows a relatively greater internal diameter: the external diameter is 4 mm, while the internal

* Supplied by J.B. Masters Ltd.

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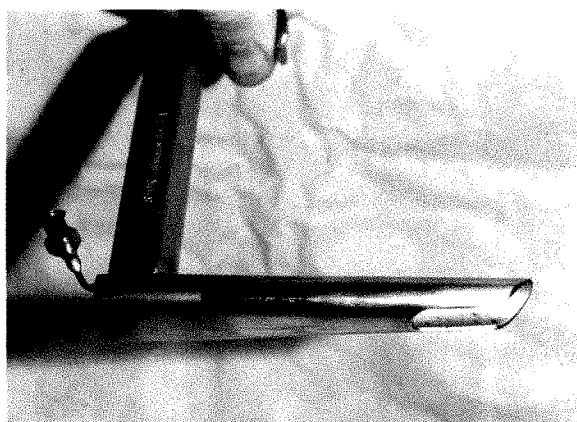


Fig. 2. The modified laryngoscope.

is 3.25 mm. The flexible portion gives ease of intubation and makes the tube more versatile. The tip is rounded to avoid possible trauma at intubation, and two additional holes are present close to the tip, to reduce the possibility of ventilatory obstruction. The distal segment is angled to reduce pressure on the posterior wall of the trachea.

Experience with the infant tube suggested a modification to the operating laryngoscope (see Fig. 2). A slot is cut in the ventral, distal surface of a Storz laryngoscope to accommodate the infant tube. The distal end of the laryngoscope is also modified to accommodate a Venturi attachment. This modification reduces the pressure of the laryngoscope on the tube and therefore minimises possible trauma to the posterior larynx and trachea.

Anaesthetic technique

Tracheal intubation severely restricts surgical access in paediatric laser surgery for removal of congenital laryngeal papillomata. The posterior larynx is completely inaccessible, as is the subglottic area. Extubation alternated with short apnoeic periods may be employed. However, this technique does not lend itself to prolonged surgery. Ventilation using a suitably sized Venturi may alternatively be employed to permit surgical access. The author endorses the technique described in 1976 by Norton⁷ which involves intubation for the initial surgery and completion of the surgery with extubation and Venturi ventilation.

Anaesthesia is induced with thiopentone and intubation with the Oswal-Hunton tube is facilitated with suxamethonium. At this time an assessment is made of the leak around the tracheal tube: if it is large, a pharyngeal pack is inserted until the surgeon is ready to place the operating laryngoscope. The pack is then removed and small soaked gauze squares, with wires attached, are placed beyond the larynx to reduce the leak when the laryngoscope is in position. Usually, however, the initial leak is small and surgery proceeds. Muscle relaxation may be maintained by further suxamethonium or by an appropriate non-depolarising drug. The tracheal tube is removed when the initial surgery is complete and a 16-gauge Venturi attached to the laryngoscope. Ventilation for the remaining surgery is by the Venturi technique with intravenous supplements of thiopentone if necessary. This is usually very much the shorter of the two surgical periods and may last only a few minutes. Long surgical sessions should be avoided in small children

since there is a greater likelihood of postoperative problems, especially laryngeal oedema. The surgical procedure should be limited to the clearance of obstructing papillomata. Patients are given dexamethazone and post-operative humidification to reduce postoperative problems.

Discussion

Venturi jet ventilation allows delivery of a ventilating gas without the need for a tracheal tube. An appropriate size of Venturi needle must be selected. The physiology and mechanics of Venturi jet ventilation delivered through an operating laryngoscope, have been described.¹² However, several complications are reported.⁷ Jet ventilation in the presence of upper airways obstruction may cause a trap-door effect with subsequent failure to ventilate. Inadequate ventilation, pneumothorax and pneumomediastinum can occur. A misdirected jet of oxygen could cause serious tracheal mucosal and paratracheal plane dissection. More commonly, it may result in gastric distension and regurgitation. Spread of particulate material, smoke and blood into the tracheobronchial tree is possible. Maximal air entrainment occurs in the initial phase of inspiration. Ruder *et al.*¹³ advised jet ventilation between, and not during periods of laser vaporisation. Laser surgery is also inadvisable during this phase since the effect of the beam is enhanced by both oxygen enrichment and the rate of gas flow. Finally, the inspiratory phase causes vibration of the vocal cords, which may be detrimental to precise surgical ablation. Large obstructing laryngeal lesions and poor lung or chest compliance may limit the use of the technique.

Anaesthesia for congenital laryngeal papillomata is a formidable problem. No single method of general anaesthesia is suitable for every patient. This is borne out by the various methods advocated. Metal tracheal tube anaesthesia in conjunction with a Venturi technique has proved to be a practical and safe technique in the authors' hands.

References

1. FRIED MP. A survey of the complications of laser laryngoscopy. *Archives of Otolaryngology* 1984; **110**: 31-34.
2. BURGESS GE III, LEJEUNE FE. Endotracheal tube ignition during laser surgery of the larynx. *Archives of Otolaryngology* 1979; **105**: 561-2.
3. SCHRAMM VL JR, MATTOX DE, STOOL SE. Acute management of laser-ignited intratracheal explosion. *Laryngoscope* 1981; **91**: 1417-26.
4. ANDREWS AH JR, MOSS HW. Experiences with the carbon dioxide laser microsurgery on the larynx. *Annals of Otolaryngology and Rhinology* 1974; **83**: 462-70.
5. SNOW JC, KRIPKE BJ, STRONG MS, JAKO GJ, MEYER MR, VAUGHAN CW. Anaesthesia for carbon dioxide laser microsurgery on the larynx and trachea. *Anesthesia and Analgesia* 1974; **53**: 507-12.
6. STRONG MS, JAKO GJ. Laser surgery in the larynx: early clinical experience with continuous CO₂ laser. *Annals of Otolaryngology, Rhinology and Laryngology* 1972; **81**: 791-98.
7. NORTON ML, STRONG MS, VAUGHAN CW, SNOW JC, KRIPKE BJ. Endotracheal intubation and Venturi (jet) ventilation for laser microsurgery of the larynx. *Annals of Otolaryngology, Rhinology and Laryngology* 1976; **85**: 656-63.
8. HUNTON J, OSWAL VH. Metal tube anaesthesia for ear, nose and throat carbon dioxide laser surgery. *Anaesthesia* 1985; **40**: 1210-2.
9. NORTON ML, DE VOS P. New endotracheal tube for laser surgery of the larynx. *Annals of Otolaryngology, Rhinology and Laryngology* 1978; **87**: 554-7.

10. VERSICHELEN L, ROLLY G, BEERENS J. Alfentanyl/etomidate anaesthesia for endolaryngeal microsurgery. *Anaesthesia* 1983; **38** (Suppl.): 57-60.
11. KAEDER CS, HIRSHMAM CA. Acute airway obstruction: a complication of aluminium tape wrapping of tracheal tubes in laser surgery. *Canadian Anaesthetists' Society Journal* 1979; **26**: 138-9.
12. WOO P, EURENIUS S. Dynamics of Venturi jet ventilation through the operating laryngoscope. *Annals of Otolaryngology and Laryngology* 1982; **91**: 615-21.
13. RUDER CB, RAPHEAL MA, ABRAMSON AL, OLIVERIO RM JR. Anaesthesia for carbon dioxide laser microsurgery of the larynx. *Otolaryngology and Head and Neck Surgery* 1981; **89**: 732-7.

APPARATUS

A comparison of different methods of lubrication of glass syringes used to identify the epidural space

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B. D. BUTLER

Summary

Measurement of loss of resistance in glass syringes is a method widely used to locate the epidural space in epidural anaesthesia. Static and dynamic forces were measured under four experimental conditions in new glass syringes: unpolished, dry; polished, dry; unpolished, saline lubricated; and polished, saline lubricated. The unpolished saline lubricated syringes had a mean (SD) static force of 53.18 (15.0) g and dynamic force of 40.88 (15.2) g. These values were significantly greater than for polished dry syringes where the values were 5.27 (2.1) g and 4.38 (0.94) g, respectively. The results show that the least amount of resistance to plunger movement is obtained by dry polishing glass syringes.

Key words

*Anaesthetic techniques; epidural, loss of resistance.
Equipment; syringes.*

Successful epidural anaesthesia depends on the accurate location of the epidural space. Doughty¹ described three distinct errors which increase the incidence of accidental dural puncture while the epidural space is located. One of these was 'the failure of the "indicator equipment" signalling the entry of the needle point into the epidural space'. This emphasises the importance of using high quality equipment when the procedure is performed. Three methods have been widely used to locate the epidural space. Two methods rely on a fluid-filled syringe (either air or saline) and the loss of resistance to injection as the needle point penetrates the ligamentum flavum and enters the epidural space. The third uses the movement of a hanging drop of liquid (at the hub of the needle) into the epidural space to indicate that the lower pressure of the epidural space has been reached.

It is generally accepted that the success of the loss of resistance technique depends greatly on the quality of the glass syringe used, which imparts sensitivity to the operator's hands. Specifically, there should be minimal resistance to movement of the plunger within the syringe barrel. Stickiness of the plunger would conversely be highly undesirable. Some operators believe that wetting the plunger before insertion into the barrel lessens this resistance and makes motion of the plunger within the barrel smoother.²

The purpose of this study was to determine whether the resistance to plunger motion can be decreased by polishing the plunger within the dry syringe barrel compared to wetting the plunger.

Methods

A new 5-ml glass syringe taken from a standard epidural anaesthesia tray (Deseret) was used for each experiment. Lubrication of the syringes was achieved by dry polishing the plunger in the barrel or by dipping the plunger and barrel into saline to wet both components thoroughly. The dry polishing was done by inserting the plunger fully into the barrel of the syringe and then rotating the barrel for five full revolutions in both directions around the plunger which was held stationary. There were four experimental conditions and four syringes were studied in each group as follows: unpolished and dry; polished and dry; unpolished and saline lubricated; and polished and saline lubricated.

The experiment was performed by mounting the barrel of each syringe in the horizontal position on a Sage 351 syringe pump (Fig. 1). The plunger, which was inserted fully into the barrel, was connected to a force transducer (Grass 10D) by a nonelastic thread attached to the end. The force transducer was connected to a chart recorder (Gould 2400) to measure the force required to withdraw the plunger from

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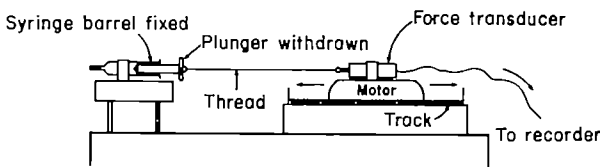


Fig. 1. Device to measure force of resistance. New glass syringe barrels are fixed and the plunger withdrawn to measure static force of resistance (fs) and dynamic force of resistance (fd).

the barrel of the syringe. The plunger was withdrawn from the barrel at a constant rate of 6.5 cm/minute. Two separate force measurements were recorded: the first was the static force of resistance (fs) which was recorded at the moment when movement of the plunger began; the second was the dynamic force of resistance (fd) which was the steady state force required to overcome the resistance while the plunger was withdrawn from the barrel. (Fig. 2).

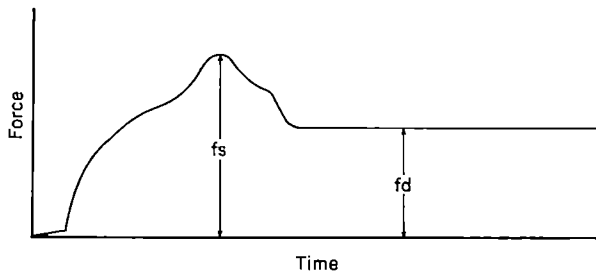


Fig. 2. Diagrammatic tracing of analogue recording which shows point of measurement of fs and fd.

All measurements were conducted at room temperature. Data were analysed using two-way analysis of variance and statistical significance determined with the Bonferroni test for multiple comparison: $p < 0.05$ was considered to be significant.

Results

Polishing of the plunger in the barrel of the syringe reduced fs and fd significantly. This applies to both dry and saline lubricated polishing and the results are shown in Table 1.

Discussion

The successful performance of epidural anaesthesia depends upon the accurate location of the epidural space. The loss of resistance technique is based upon the compression of air or saline within a syringe while the needle is located in the ligamentum flavum. Resistance to the syringe plunger is lost as the needle penetrates the epidural space. Inadvertent puncture of the dura mater may occur if the resistance to movement of the plunger is high, since the sensitivity of the technique is diminished.

Bromage² recommended that the barrel and plunger of the syringe be wetted to reduce friction. We demonstrated

Table 1. Static and dynamic forces (grams, SD).

	Static force of resistance (fs)	
	Unpolished (n = 4)	Polished (n = 4)
Dry	11.38 (3.48) ^b	5.27 (2.09) ^a
Wet	53.18 (15.04)	28.07 (7.68) ^{cd}
	Dynamic force of resistance (fd)	
	Unpolished (n = 4)	Polished (n = 4)
Dry	8.16 (3.28) ^b	4.38 (0.94) ^a
Wet	40.88 (15.17)	19.88 (4.21) ^{cd}

Data are means (SD)
a $p < 0.05$ comparing polished dry to unpolished wet
b $p < 0.05$ comparing unpolished dry to unpolished wet
c $p < 0.05$ comparing unpolished dry to polished wet
d $p < 0.05$ comparing polished dry to polished wet

that the greatest resistance to plunger movement occurred in unpolished saline lubricated syringes (fs 53.18 (15.0) g, fd 40.88 (15.2) g) while the lowest resistance occurred in polished dry syringes (fs 5.27 (2.1) g, fd 4.38 (0.94) g).

The force required to move the syringe plunger is equal in magnitude and opposite in direction to the force of resistance imparted by contact of the plunger with the barrel. New ground-glass syringes are not smooth but contain microscopic peaks and valleys. The peaks come into contact with the opposing glass wall to produce friction. The valleys which do not contact the opposing wall do not contribute to friction. Saline immersion may increase friction by one of several mechanisms. The saline may fill the microscopic valleys so that the area of surface contact is increased or negative pressure may be generated in the valleys as the plunger passes through the barrel in a saline filled system. Further considerations may include the effects of fluid surface tension and viscosity on the saline lubricated plunger. Polishing smooths the surface, reduces the peaks and decreases friction. The plunger was withdrawn from the syringe barrel at a constant rate in the present study. This motion is opposite to conditions of use but the net force of resistance is the same whether the plunger is pushed or pulled. Other problems encountered in clinical practice that are not related to friction include situations where the plunger becomes jammed in the syringe barrel due to poor fit or contamination with talcum powder.

Acknowledgment

The authors thank Mrs M. Choate for typing this manuscript.

References

1. DOUGHTY A. A precise method of cannulating the lumbar epidural space. *Anaesthesia* 1974; 29: 63.
2. BROMAGE PR. *Epidural anaesthesia*. Philadelphia: W.B. Saunders, 1978: 195.

APPARATUS

Cuff failure in polyvinyl chloride tracheal tubes sprayed with lignocaine

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Summary

The incidence of tracheal tube cuff rupture was noted in 30 polyvinyl chloride tracheal tubes lubricated with three different solutions. All cuffs moistened with water were intact after 2 hours of cuff inflation whereas two of 10 lubricated with 4% lignocaine solution had burst. Both of these had leaked at the site of cuff attachment to the tube. Fifty percent of tubes lubricated with Astra lignocaine spray burst during the study. Four of the five had developed pinholes in the cuffs themselves. The remaining 50% of this group showed marked distortion and thinning of their intact cuff walls. The implications of these findings are discussed in view of the widespread use of PVC tracheal tubes.

Key words

Anaesthetics, local; lignocaine spray.

Equipment; tubes, tracheal.

Recent emphasis on economy led our group of hospitals to change to our standard tracheal tube. The Portex standard cuff Theatre Tube was chosen after various tenders, representing a saving of some 50% on the tubes used previously. It was felt within weeks of using the new stock, that more cuffs had burst than would normally be expected. This study was designed to determine whether the Portex Theatre Tube cuff is more likely to burst than the Portex Blue Line cuff and whether either 4% lignocaine solution or Astra lignocaine spray contributes to this incidence.

Methods

Fifteen Portex Theatre Tubes were divided into three groups of five. Each group contained one tube from each of five different batches in order to avoid any defects peculiar to a batch. Fifteen Portex Blue Line tubes were selected and divided likewise. All tubes were 8.5 mm in diameter and were lubricated for about 10 seconds in the following manner: group A, 2 ml water; group B, 2 ml 4% lignocaine solution (as hydrochloride with 0.1% chlorocresol); group C, five spray doses of Astra lignocaine spray (lignocaine 10% w/v with cetylpyridinium chloride 0.0001%).

The cuffed end of each tube was then inserted into the proximal end of the barrel of a 10-ml Gillette Sabre syringe from which the plunger was removed. The other end of the tube was occluded by a rubber bung. A cuff syringe (Fig. 1, A) was used in the normal fashion until there was

no leak when tested by a second syringe (Fig. 1, B). This was attached by plastic tubing to the distal end of the syringe barrel that contained the cuff. Each syringe barrel, complete with tube, was then submerged upright in a water bath at 37°C such that the water level was above the whole barrel. With this arrangement a pocket of air remains trapped in the barrel below the cuff of each tube. This air is released if the cuff deflates and the resulting bubbles indicate cuff deflation. The time at which any cuff burst was noted.

All the remaining intact cuffs were inflated with a further 5 ml of air after one hour, without disturbing the tubes in the water bath. This was considered to be a good test of any cuff weakness that may have developed. These tubes were left submerged for another hour and any further cuffs that burst were noted.

All remaining intact cuffs were deflated at the end of the second hour. All the tubes were removed from their syringe barrels, their cuffs re-inflated and examined carefully. The sites of the cuff leaks were noted, as was any distortion of the remaining intact cuffs.

All results were analysed using the Chi-squared test.

Results

Incidence of total cuff failure

There was no statistical difference in the incidence of burst cuffs between the Blue Line and the Theatre Tube groups

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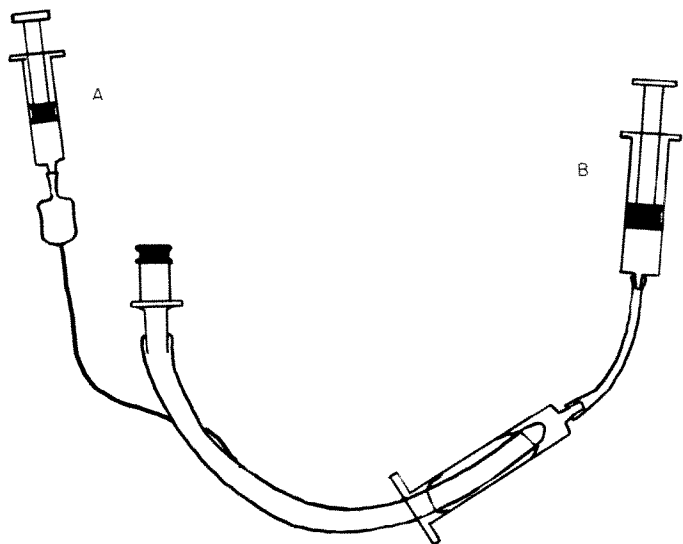


Fig. 1. Details of experimental method. The tracheal tube connector is occluded by a black rubber bung and its cuffed portion inserted into a syringe barrel. The cuff was inflated with air using syringe A until there was no leak as tested by syringe B.

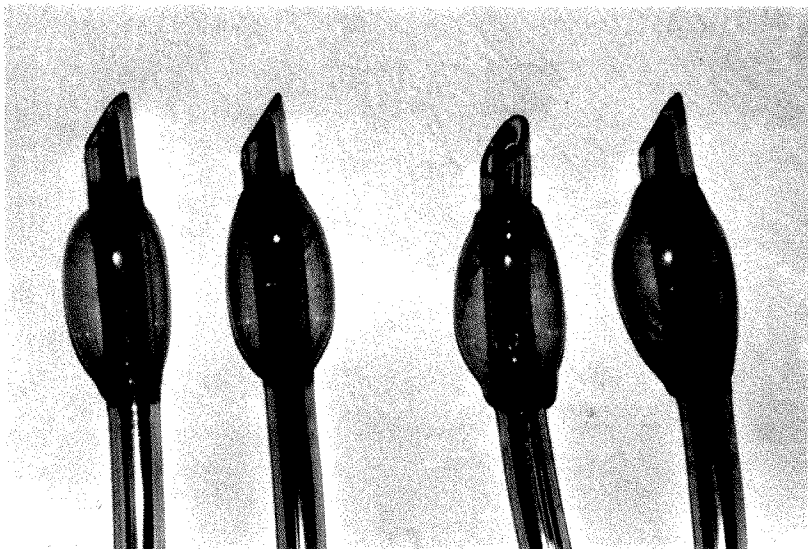


Fig. 2. The two normal cuffs on the left were lubricated with water. The two on the right show partial seam detachment and distortion of the cuffs after lubrication with Astra lignocaine spray.

Table 1. The incidence of cuff failure in Theatre Tube and Blue Line tracheal tubes when lubricated with water, 4% lignocaine and Astra lignocaine spray.

	Blue Line	Theatre Tube	Total (n = 10)
Group A (water)	0	0	0
Group B (lignocaine 4%)	1	1	2
Group C (lignocaine spray)	3	2	5
Total (n = 15)	4	3	

(Table 1). There was, however, a notable difference of cuff failure between the three lubricant groups. The difference between groups A and C was statistically significant ($p < 0.05$) whilst other differences were not.

Site of cuff failure

Cuff failure fell into two categories: pinhole defects in the cuff wall, and seam leakage at the site of cuff attachment to the tube. Both of the group B failures were due to seam leakage. Four of the five failures in group C were due to pinhole defects in the cuff itself and only one was due to seam leakage.

Results of inspection of remaining intact cuffs

There were 23 intact cuffs: 10 in group A, eight in group B and five in group C. None of the 10 cuffs in group A showed any abnormality on re-inflation. Two of the eight in group B showed partial seam detachment without actual leakage. The remaining six appeared to be normal. All five intact cuffs in group C showed both marked partial seam detachment and distortion, and apparent thinning of the cuff (Fig. 2). One of these burst on re-inflation.

Discussion

There was no difference in the incidence of cuff failure between the Portex Blue Line tube and the less expensive Portex Theatre Tube. However, the use of some lubricants greatly increased the incidence of cuff failure, most notably the Astra lignocaine spray. Fifty percent of the tubes in this group developed complete cuff failure whilst the remaining 50% showed marked abnormalities of the seam attachment, and distortion and thinning of the cuff itself.

It has been shown that lignocaine base aerosol can cause blistering, pinholes and sudden rupture of PVC cuffs.¹ All of these features occurred in this study in group C. It has been suggested that the aerosol contains a swelling agent which softens the cuff and this leads to blistering and rupture.¹ We understand that Astra Pharmaceuticals Ltd are likely to issue a warning about the use of lignocaine spray

with PVC cuffs (personal communication). Lignocaine 4% topical and 2% gel, both of which contain the salt and not the base, are suggested alternatives.¹ This study shows that although none of the cuffs sprayed with topical lignocaine 4% developed holes or blisters, two developed leaks in the seam attachment of the cuff to the tube and a further two showed signs of abnormal seams. This incidence is of clinical importance.

Spraying the larynx with local anaesthetic is practised widely in anaesthesia but it appears that great care needs to be taken. Astra Pharmaceuticals Ltd lignocaine spray leads to widespread distortion and failure of PVC cuffs. In the authors' opinion it should not be used with these types of tubes. Topical lignocaine 4% is better and does not appear to affect the cuff itself but there may still be an incidence of cuff failure. This may exclude its use in clinical situations where the need for urgent re-intubation may be hazardous to the patient or difficult for the anaesthetist once surgery has begun. The use of non-PVC tracheal tubes should be considered if local anaesthesia of the larynx is desirable.

Reference

1. JAYASURIYA KD, WATSON WF. P.V.C. cuffs and lignocaine-base aerosol. *British Journal of Anaesthesia* 1981; **53**: 1368.

Pulse oximetry and postoperative hypothermia

An evaluation of the Nellcor N-100 in a cardiac surgical intensive care unit

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Summary

The accuracy of the Nellcor N-100 pulse oximeter was evaluated in hypothermic patients (core temperature $\leq 35.0^{\circ}\text{C}$) after cardiac surgery. The pulse oximeter overestimated oxygen saturation in comparison to values obtained by direct in vitro oximetry with a mean bias of 0.6% saturation. The 95% predictability limits for individual measurements were $\pm 3.9\%$ oxygen saturation. No demonstrable loss of accuracy was caused by skin pigmentation, the concurrent administration of low doses of dopamine or vasodilators, or the intra-operative intravascular administration of Patent Blue V dye.

Key words

*Hypothermia; postoperative.
Measurement techniques; pulse oximetry.*

The dangers of relying on clinical observation for the detection of hypoxaemia have long been recognised. The recent introduction of pulse oximetry has provided a reliable, noninvasive and convenient method suitable for the routine monitoring of arterial haemoglobin oxygen saturation (SaO_2).¹ The Nellcor N-100 pulse oximeter has been evaluated in healthy volunteers² and in routine anaesthetic and intensive care practice,³⁻⁵ and has been shown to be a reliable early detector of arterial oxygen desaturation.

Pulse oximeters function by electronic comparison of the degree of absorption of two light wavelengths (one red and one infrared) by interposed pulsatile tissues. It has been suggested that a reduction in the amplitude of vascular pulsations, such as may occur during the infusion of vasoconstrictor drugs or in association with hypothermia, would result in a loss of accuracy of the instrument.^{2,3} Patients submitted to surgery are frequently hypothermic in the operating theatre and recovery room. The purpose of the present study was to evaluate the Nellcor N-100 pulse oximeter (Nellcor Inc., Hayward, California) in patients who had undergone cardiac surgery. Mild hypothermia is relatively common in such patients and the temperatures encountered represent the extremes of postoperative hypothermia in non-cardiac anaesthetic practice.

Methods

Twenty-one patients participated in the study, which was approved by the Ethics Committee of the National Heart

Hospital. All received mechanical ventilation of the lungs after coronary artery bypass surgery or heart valve replacement that involved cardiopulmonary bypass, the use of cold cardioplegia solution and topical myocardial cooling. They were consequently hypothermic (core temperature $\leq 35.0^{\circ}\text{C}$). All patients had a radial arterial cannula *in situ* for routine monitoring and required regular arterial blood sampling during their postoperative management. The pulse oximeter finger sensor was attached to the index finger of the hand supplied by the cannulated radial artery. When a stable Sao_2 reading was obtained, blood was withdrawn from the radial artery cannula for immediate direct measurement of haemoglobin saturation (Radiometer OSM2, Radiometer, Copenhagen) and blood gas estimation (ABL30, Radiometer, Copenhagen). Heart rate and rhythm, arterial pressure, core and peripheral temperatures and drug therapy were noted at the time of sampling. No more than four samples were taken from each patient.

The Radiometer OSM2 automated oximeter has been evaluated previously and found to produce results in close agreement with those obtained using an absolute method of oxygen content analysis.⁶ Core and peripheral temperatures were measured using rectal and cutaneous (finger) thermistors (Simonsen & Weel, Sidcup, Kent). These were calibrated against a National Physical Laboratory mercury-in-glass total immersion thermometer in a stirred water bath, and were accurate to $\pm 0.3^{\circ}\text{C}$ over the temperature range studied.

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Results

Sixty-eight paired estimations of arterial blood haemoglobin saturation were made in 21 patients whose core temperatures ranged from 32.3 to 35.0°C. The clinical data are shown in Table 1. *In vitro* haemoglobin saturation

Table 1. Summary of clinical data.

	Range	Mean	Standard deviation
Age (years)	47–68	59.5	6.9
Systolic arterial pressure (mmHg)	90–140	99.0	18.2
Heart rate (beats/minute)	71–148	118.0	13.0
Haemoglobin (g/dl)	7.8–11.5	10.1	0.76
Arterial pH	7.19–7.57	7.39	0.08
PaO ₂ , kPa	6.84–34.66	17.20	6.13
Paco ₂ , kPa	3.00–7.85	4.77	1.01
Core temperature (°C)	32.3–35.0	34.2	0.65
Finger temperature (°C)	24.4–30.6	26.6	1.49

ranged from 89.9% to 99.9%. Four of the 21 patients studied (14 estimations) had racially pigmented skin and 11 (37 estimations) received between 25 and 50 mg intra-arterial Patent Blue V dye (May & Baker, Dagenham, Essex) intra-operatively as part of the surgical technique. Three patients (10 estimations) received an intravenous infusion of glyceryl trinitrate (GTN) at up to 1 µg/kg/minute; three patients (11 estimations) received an infusion of sodium nitroprusside (SNP) at up to 1 µg/kg/minute; and three patients (nine estimations) received a dopamine infusion at up to 5 µg/kg/minute. A further two patients (four estimations) received complex drug therapy with dopamine, GTN and adrenaline combinations. None of the patients was hypotensive (systolic arterial pressure <90 mmHg) and all except one were in sinus rhythm throughout the period of the study.

Signal failure occurred in two patients. No stable signal could be obtained in one patient until the core temperature rose above 35.0°C. Signal failure occurred in the second patient at a core temperature of 32.3°C when an SNP infusion was reduced from 1 µg/kg/minute to 0.5 µg/kg/minute. The signal reappeared when the higher infusion rate was resumed. Transient atrial fibrillation occurred in one patient at the time of blood sampling; the pulse oximeter displayed a pulse rate of 80 beats/minute during the dysrhythmia, when the true ventricular rate was 140 beats/minute.

Data analysis was by the method of Bland and Altman⁷ for the assessment of agreement between two methods of measuring the same quantity. An estimate of bias is given by the mean of the differences between measurements, and a plot of the differences against the mean values permits assessment of bias throughout the range studied. A paired *t*-test on the mean difference compared with a mean of zero gives a value for the probability of inherent bias in one method compared with the standard. These data are summarised in Table 2. The results indicate that the Nellcor N-100 over-read compared with the Radiometer OSM2 with a mean difference of 0.6% oxygen saturation. Detailed analysis of the data did not reveal any statistically significant bias attributable to pigmented skin, dopamine, vasodilators or Patent Blue V dye.

Individual measurements are represented graphically in Fig. 1. Linear regression analysis shows that the 95% pre-

Table 2. Summary of statistics on differences between pairs of saturation measurements, sat(Nellcor) – sat(OSM2).

Number	68
Mean difference	0.6%
Standard deviation	1.6%
Standard error of the mean	0.2%
95% confidence interval for mean	0.2–1.0%
Paired <i>t</i> -test on difference, mean = 0	<i>p</i> < 0.005

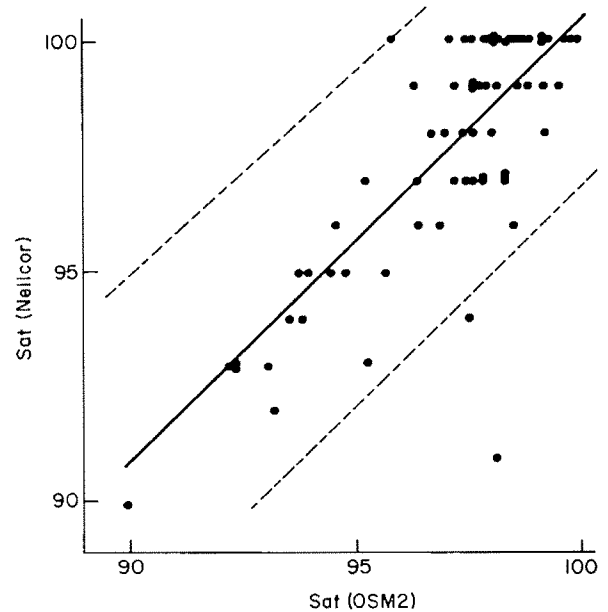


Fig. 1. Saturation measured by Radiometer OSM2 (Sat(OSM2)) and Nellcor N-100 (Sat(Nellcor)). The linear regression line (solid) and 95% prediction limits (hatched) are shown ($r = 0.73$, $p < 0.001$; $y = 0.95x + 5.45$).

diction limits differ from the calculated linear regression line by no more than 3.9% oxygen saturation. The prediction interval has been used since this is wider than the confidence interval and gives a better indication of the certainty with which a true SaO_2 value may be predicted from a single SaO_2 measurement made by the pulse oximeter. These data indicate that individual measurements of SaO_2 obtained from hypothermic patients using the Nellcor N-100 fell within the manufacturer's specified limits of accuracy (i.e. 95% confidence limits of $\pm 4\%$ oxygen saturation).

Discussion

It is well known that patients lose heat during surgery and that many are hypothermic in the operating theatre and recovery room.⁸ Postoperative hypothermia is associated with an increased risk of hypoxia due to the increased tissue oxygen demand of rewarming⁹ and the residual cardio-respiratory depressant effects of anaesthetic drugs. Pulse oximetry is potentially of benefit to these patients if the technique is accurate in the presence of hypothermia and vasoconstriction. We conclude from our data that the Nellcor N-100 provides a reliable method for the continuous monitoring of SaO_2 in the mildly hypothermic patient where an adequate signal is detected by the instrument, and that signal failure is in any case an uncommon occurrence. However, it should be borne in mind in the

interpretation of measured SaO_2 values that the arterial oxygen tension which corresponds to a given saturation may be significantly lower than at normothermia, due to the leftward shift of the haemoglobin dissociation curve at low temperatures. This, in part, accounts for the narrow, relatively high range of saturations observed in this study and means that a decrease in arterial oxygen tension will be detected later by pulse oximetry in hypothermic than in normothermic patients.

Data on pulse oximetry in peripherally vasoconstricted patients are scarce and the late effects of the systemic administration of dyes on the accuracy of pulse oximeters has not to our knowledge been investigated previously. Signal failure occurred in two of nine patients who received vasopressors in a previous study³ but there was no loss of accuracy in the other measurements. However, Tremper *et al.*¹⁰ reported a tendency for the pulse oximeter to over-read in 12 out of 14 samples taken from patients with a high systemic vascular resistance index. Our findings confirm that the Nellcor N-100 slightly overestimates the true value of SaO_2 in the vasoconstricted patient. This, combined with the leftward shift of the haemoglobin dissociation curve already mentioned, leads us to recommend that the low alarm be set at a higher level in the hypothermic patient than the value of 94% SaO_2 which was suggested recently for routine use.¹¹

Infusions of dopamine did not seem to affect the accuracy of the Nellcor N-100 in the present study; the small doses used are unlikely to have caused a further decrease in peripheral vascular pulsation. Pulse oximeter signal failure has been reported with doses of dopamine as low as 7 µg/kg/minute³ and it is likely that some loss of accuracy will result if higher doses of the drug are given.

Vasodilator therapy in the coldest patient studied (core temperature 32.3°C), improved signal detection despite the small dose given. In view of the satisfactory overall performance of the Nellcor N-100 we are unable to reach any conclusions about the facilitation of pulse oximeter accuracy by vasodilators on the basis of this one observation.

Blue dyes administered intravascularly or topically are popular in some surgical subspecialties. Patent Blue V is similar to the more widely available Methylene Blue. Our failure to demonstrate any significant effect of Patent Blue V on the accuracy of the Nellcor N-100, may be ascribed to the low absorbance of the dye at the wavelengths used by the instrument (660 and 925 nm) and to the relatively small dose. The Radiometer OSM2 uses wavelengths of 505 and 600 nm, at which absorbance due to Patent Blue V is unlikely to distort SaO_2 measurements. We conclude that the administration of blue dyes, particularly if used topically, is not likely to cause a significant loss of accuracy in estimations of SaO_2 made by the Nellcor N-100 unless considerable methaemoglobinaemia is present.³

The agreement found between the values of SaO_2 measured by pulse oximetry and *in vitro* oximetry in this study is similar to that described by previous investigators in normothermic patients.^{4,5,10} Our results show that mild postoperative hypothermia does not have a significant effect upon the accuracy of the Nellcor N-100. Any potential limitation to the usefulness of pulse oximetry for the detection of arterial desaturation in the mildly hypothermic patient is likely to be determined by physiological changes in the haemoglobin dissociation curve, rather than by the instrument itself.

Acknowledgments

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References

1. HANNING CD. Monitoring oxygenation during anaesthesia. *British Journal of Anaesthesia* 1985; **57**: 359–60.
2. YELDERMAN M, NEW W. Evaluation of pulse oximetry. *Anesthesiology* 1983; **59**: 349–52.
3. MIHM FG, HALPERIN BD. Noninvasive detection of profound arterial desaturations using a pulse oximetry device. *Anesthesiology* 1985; **62**: 85–7.
4. TYTLER JA, SEELEY HF. The Nellcor N-101 pulse oximeter. A clinical evaluation in anaesthesia and intensive care. *Anaesthesia* 1986; **41**: 302–5.
5. FANCONI S, DOHERTY P, EDMONDS JF, BARKER GA, BOHN DJ. Pulse oximetry in pediatric intensive care: comparison with measured saturations and transcutaneous oxygen tension. *Journal of Pediatrics* 1985; **107**: 362–6.
6. SALOOJEE Y, COLE PV, ADAMS L. The evaluation of a photometer (the Radiometer OSM2) for the determination of haemoglobin concentration and per cent oxyhaemoglobin and carb-oxyhaemoglobin in blood. *Journal of Medical Engineering and Technology* 1981; **5**: 298–300.
7. BLAND JM, ALTMAN DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307–10.
8. VALE JR. Normothermia, its place in operative and post-operative care. *Anaesthesia* 1973; **28**: 241–5.
9. ROE CF, GOLDBERG MJ, BLAIR CS, KINNEY JM. The influence of body temperature on early postoperative oxygen consumption. *Surgery* 1966; **60**: 85–92.
10. TREMPER KK, HUFSTEDLER SM, BARKER SJ, ADAMS AL, WONG DH, ZACCARI J, BENIK K, LEMONS V. Accuracy of a pulse oximeter in the critically ill adult: effect of temperature and hemodynamics. *Anesthesiology* 1985; **63**: A175.
11. TAYLOR MB, WHITWAM JG. The current status of pulse oximetry. Clinical value of continuous noninvasive oxygen saturation monitoring. *Anaesthesia* 1986; **41**: 943–9.

APPARATUS

A drawover Boyle's machine

Development and evaluation in Zambia

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Summary

A standard Boyle International anaesthetic machine was modified to allow operation in either a continuous flow or a drawover mode. This was achieved by fitting a valve in the backbar which allows entrainment of air under drawover conditions. The details of the valve and modification are discussed and an evaluation of the machine in a Central African hospital is presented.

Key words

Equipment; anaesthetic machine, vaporizers.

Most developed countries during the past 30 years have adopted continuous flow methods of anaesthesia which have largely replaced drawover techniques except in military or emergency situations. Many developing countries have followed this trend and serious problems have frequently arisen because of the absence of routine maintenance and difficulties in ensuring adequate supplies of compressed gases to remote parts of the country. It is well known that drawover anaesthesia in countries such as Zambia has advantages in terms of both cost and logistics.¹ Anaesthetic services nevertheless commonly depend on Boyle's machines* since there is very little access to draw-over apparatus. In order to address this problem we modified a Boyle International anaesthetic machine to permit it to be used in either a continuous flow or a draw-over mode.

Methods

A Boyle International anaesthetic machine which was in good working order was chosen for modification. The vaporizer was removed and a valve developed by Dr J. Zorab, which allows the backbar to open to atmosphere, was fitted to the downstream side of the Rotameter block (Fig. 1). This requires simple modification of the backbar of the machine which was cut and a steel plate welded in place to form a recess which accommodated the width of the valve.

The valve is a simple gravity-operated flap valve (Figs 1 and 2) which allows air to be drawn into the backbar when the pressure becomes subatmospheric. This allows the machine to be used in either a continuous flow or a draw-

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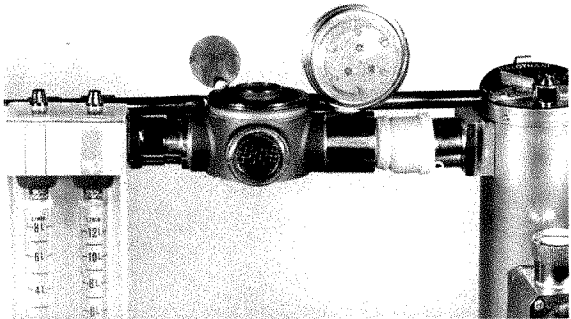


Fig. 1. The flap valve mounted on the backbar of the Boyle's machine.

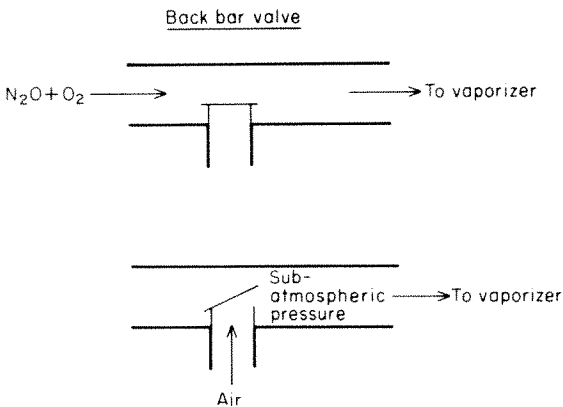


Fig. 2. The function of the flap valve during continuous flow and drawover modes.

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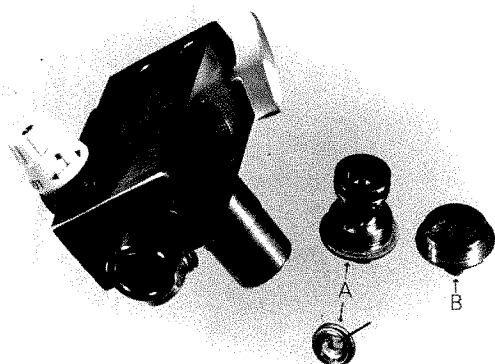


Fig. 3. Modified backbar pressure relief valve. (A) Needle valve and retaining screw; (B) modified valve.

over mode. An Oxford Miniature Vaporizer (OMV 50),† whose performance is adequate in either continuous flow or drawover mode,² was fitted to the backbar immediately downstream of the air-entraining valve to allow vaporization of halothane.

The emergency oxygen/backbar pressure relief valve was modified to ensure that the resistance to respiration was acceptable for drawover anaesthesia by dismantling the valve assembly (Fig. 3), removing the needle valve and cutting the retaining screw for the valve (A in Fig. 3); this disables the valve and increases the overall internal diameter. Figure 3 (B) shows the modified valve.

A series of simple experiments was conducted to assess the resistance to gas flow in the drawover mode. A suitable range of gas flows was produced by an electrically driven clinical suction unit connected to the common gas port of the machine. The pressure drop was recorded for a range of continuous gas flows with a water manometer connected to the common gas outlet, and gas flows were measured with a Wright's respirometer attached to the inlet port of the backbar valve. The measurements were repeated with three healthy volunteers and then 10 anaesthetised patients who breathed through the machine.

The machine was then equipped with two anaesthetic breathing systems: a Magill for continuous flow anaesthesia (Fig. 4), and a Triservice system that comprised a Laerdal resuscitation bag and anaesthetic non-rebreathing valve for drawover anaesthesia³ (Fig. 5). At least 1 litre/minute of oxygen was added to the inspired gases via the Rotameter during drawover anaesthesia; this amount was increased for pre-oxygenation and in high-risk cases. A Heidbrink valve was attached to the common gas outlet of the machine to allow any excess pressure in the backbar to escape and thus to prevent a build up of pressure in the inspiratory limb during drawover anaesthesia.

The first 100 patients anaesthetised with the machine at the University Teaching Hospital, Lusaka, were studied to investigate any problems associated with the use of the machine in either the continuous flow mode with nitrous oxide, oxygen and halothane, or the drawover mode with air, oxygen and halothane. It was impossible to randomise these patients because of shortages of nitrous oxide. A standard proforma was completed for each anaesthetic that gave details of the patient, operation, recovery and any problems that arose during the procedure. Anaesthesia was

† Penlon Ltd, Radley Road, Abingdon OX14 3PH, UK.

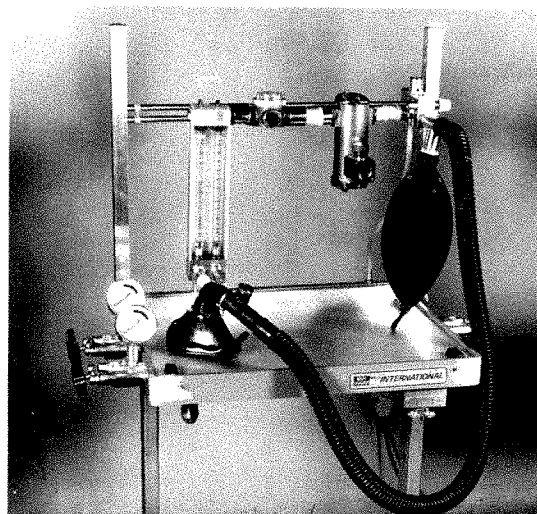


Fig. 4. Modified Boyle's machine with Magill breathing system.

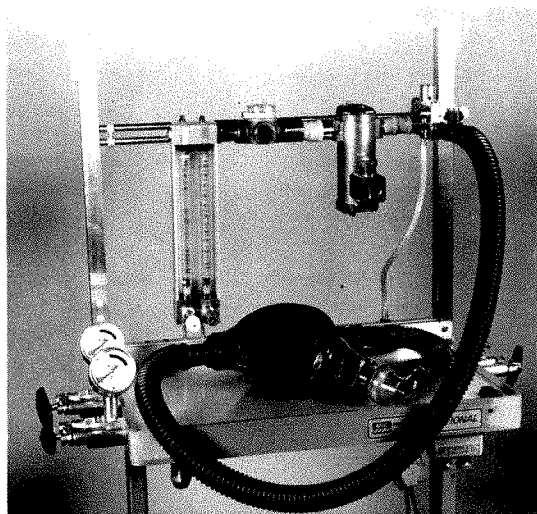


Fig. 5. Modified Boyle's machine with Triservice breathing system incorporating a Heidbrink valve at the common gas outlet.

administered by a range of anaesthetists graded from consultant to student clinical officer under supervision. The anaesthetist assessed the machine as good, adequate or poor at the end of each case.

Results

The pressure drop produced in the modified machine at the various continuous gas flows generated is shown in Fig. 6. The pressure drop did not exceed 0.15 kPa during normal inspiration in any of the three volunteers or the 10 anaesthetised patients in whom it was recorded.

One hundred patients were anaesthetised with the machine, 50 in the drawover mode and 50 in the continuous flow mode. Mistakes were made in the selection of breathing systems on five occasions (three in the drawover group and two in the continuous flow group). Three patients in the drawover group and two in the continuous flow group were difficult to anaesthetise because of reduced halothane output that resulted from cooling of the OMV vaporizer. No other problems were noted.

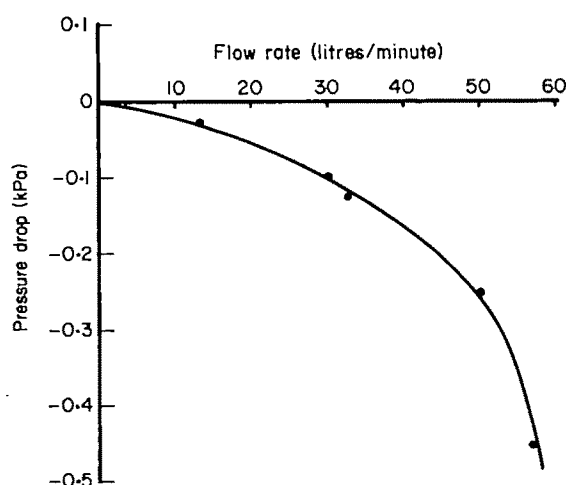


Fig. 6. The pressure drop produced by flows generated by suction applied to the common gas outlet.

The machine in the continuous flow mode was described as good in 48 cases and adequate in two. In the drawover mode it was assessed as good in 49 and adequate in one. Light anaesthesia resulted from cooling of the OMV, in the three adequate cases.

Discussion

The provision of anaesthetic services to remote parts of developing countries is frequently hampered by unreliable supplies of compressed gases, drugs and spare parts for equipment. Continuous flow anaesthetic apparatus can be a particular problem in this environment. In addition, the routine servicing which this type of equipment requires is unlikely to be carried out. Anaesthetic machine graveyards are commonplace in many parts of developing Africa and simpler drawover anaesthesia equipment such as the Tri-service apparatus or the EMO system may be more practical in these situations. However, these recommendations have not been accepted in many developing countries and anaesthetists of all grades are trained and supplied with continuous flow apparatus.

It is in this context that the concept of a drawover Boyle's machine was formulated. It is intended to allow the use of existing Boyle's machines where supplies of compressed gases are short and expertise in the maintenance of complex vaporizers is nonexistent. The modified machine could even be used without oxygen in emergency situations although this is not ideal and is likely to result in hypoxia.⁴

The machine may be combined with an oxygen concentrator in the drawover mode and, in contrast to complex plenum vaporizers, the OMV allows operator servicing. We found the machine straightforward to modify in the absence of complex engineering facilities and it may be a practical and economical method to resurrect certain redundant Boyle's machines in developing countries. Unfortunately, not all Boyle's machines are suitable for this modification since some models have narrow bore gas tubing which would result in excessive resistance to ventilation.

There are certain categories of patients who are more difficult to anaesthetise with standard drawover techniques and this is particularly important in areas where anaesthesia may be administered by inexperienced personnel. This machine allows the option of continuous flow anaesthesia

in certain cases, for example infants or neonates, while drawover anaesthesia can be employed for the majority of cases with a resultant conservation of compressed gases.

The present model of the modification is not, however, without problems. There is potential for hazardous mistakes in system selection and connexion. These mistakes in our study fell into two categories. Firstly, in the drawover mode, almost total rebreathing results if a Magill system is used in error. Secondly, when a circuit that contains a non-rebreathing anaesthetic valve is used in conjunction with a continuous flow of anaesthetic gases in either the drawover or continuous flow modes, a dangerous build up of pressure in the inspiratory limb of the circuit may result in the valve jamming during inspiration and in grave risk of pulmonary barotrauma. The machine must be used with a pressure relief valve in the patient system in the drawover mode, for example an open Heidbrink valve, in order that the patient is protected from this problem. An anaesthetic reservoir bag is also suitable provided that the pressure within is never allowed to increase; this has the advantage that it permits an oxygen reservoir to be formed which allows high concentrations of oxygen to be given. A combination of both bag and the valve is theoretically the most appropriate but is rather bulky in practice.

Systems were misconnected on five occasions during the period of our study and this is an area of concern. However, the machine has been used several times a week without further incident since this initial group of 100 patients. The need for a period of training and supervision when the machine is used, is emphasised.

We consider that the machine should be used routinely in one mode and converted to the other when a situation demands it. This reduces frequent changes of system and avoids potential confusion. If the machine were to be produced commercially the drawover system should be supplied as a separate entity with the pressure relief system built in and unable to be modified. Warning notices on the machine would be useful, both in English and a selection of appropriate local languages.

Cooling of the OMV vaporizer with a consequent decrease in output is a recognised problem and light anaesthesia was noted on five occasions in our study. This problem can be solved either by intravenous opioid supplementation or by the addition of a second vaporizer for the administration of, for example, trichloroethylene. The latter involves more expense and is probably unnecessary provided that opioids or other intravenous agents such as ketamine are available.

The machine has advantages over standard drawover equipment despite these problems. It is easy to use in a drawover mode for routine anaesthesia and the facility to change to continuous flow anaesthesia with nitrous oxide is beneficial for gaseous inductions, obstetric and neurosurgical cases. Some anaesthetists prefer to employ continuous flow techniques in paediatric anaesthesia. We have found the modified machine to be particularly applicable in our environment since several of our anaesthetists do not employ drawover techniques whereas others use them routinely and the flexibility of the apparatus is a most attractive feature.

Acknowledgments

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References

1. EZI-ASHI TI, PAPWORTH DP, NUNN JF. Inhalational anaesthesia in developing countries. Part 1. The problems and a proposed solution. *Anaesthesia* 1983; **38**: 729–35.
2. SCHAEFER H-G, FARMAN JV. Anaesthetic vapour concentrations in the EMO system. *Anaesthesia* 1984; **39**: 171–80.
3. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; **36**: 1094–1108.
4. AKINYEMI OO, ADELAJA AB. Blood gas studies using spontaneously respired halothane in ambient air. *Anaesthesia* 1982; **37**: 353–4.

Forum

One lung high frequency ventilation for peroral sealing of bronchial stump fistulae

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Summary

The use of high frequency ventilation for 28 repairs of bronchial stump fistulae with fibrin sealant is discussed. Intravenous anaesthesia with continuous infusions of methohexitone, alfentanil and suxamethonium was employed. This method of anaesthesia and ventilation proved to be satisfactory.

Key words

Anaesthetics, intravenous; methohexitone, alfentanil. Surgery; bronchial fistula.

Bronchial stump fistulae are a serious complication after pneumonectomy and their surgical repair is often difficult. Positive reports on the use of fibrin sealant in the airway^{1–4} encouraged us to use this method and to adjust our technique of anaesthesia and ventilation to this specific problem.

The possibility of sealing tissues by fibrin adhesive has been studied *in vitro* in rat skin⁵ and nerve,⁴ for tracheal repair in dogs² and for the treatment of bronchial stumps after pneumonectomy in pigs.³ In man, fibrin glue was applied successfully to treat 21 patients with pneumothorax by thoracotomy and sealing under visual control.⁶ One patient with a bronchopleural and four with other thoracic fistulae were treated in another study with sealant applied under direct vision through a conventional metallic bronchoscope.¹ The need to avoid powerful ventilation at the site of sealant application was stressed.

One lung high frequency ventilation has been used successfully for sleeve pneumonectomy.⁷ The present aim of this study was to evaluate the technique of total intravenous anaesthesia and high frequency ventilation for a relatively new kind of surgical treatment.

Methods

The fibrin sealant used (Immuno AG, Vienna, Austria) is a multicomponent biological adhesive which may effect haemostasis, seal tissue and promote wound healing. A double-barrelled syringe connected to the Tissomat apparatus (Immuno AG, Vienna, Austria) is used to apply the components.

High frequency ventilation (HFV) and total intravenous anaesthesia are used routinely for peroral diagnostic procedures and surgery in our institution.⁸ We decided to adjust this technique for use during the application of fibrin sealant to bronchial stump fistulae after pneumonectomy.

Ventilation of the lung is achieved with an Acutronic MK 800 ventilator at frequencies of 1.8–2.5 Hz, an operation pressure of 1.4–2.2 bar and an inspiratory time of 30% of the cycle. F_{IO_2} is usually set at 0.5. The insufflation

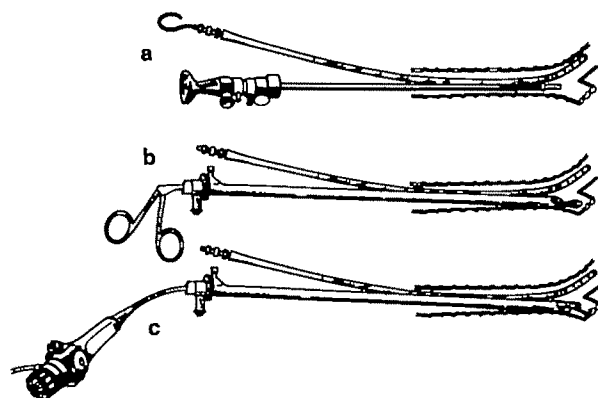


Fig. 1. Three steps when instruments are positioned in the airway to seal a fistula in the bronchial stump. (a) The insufflation catheter covered in aluminium foil is positioned in the main bronchus under direct vision using the optical stylette.¹⁰ (b) A rigid bronchoscope is introduced. A biopsy forceps is passed through the bronchoscope, and used to extract protruding sutures (if present), when possible to apply collagen haemostatic felt (B. Braun, Melsungen, FRG), which has been sprayed with sealant, into the opening of the fistula. (c) Sealant is applied through a thin rigid catheter passed through the suction channel of a flexible bronchoscope. The flexible bronchoscope is passed through the lumen of the rigid bronchoscope.

catheter is covered with a thin aluminium foil⁹ to ensure correct positioning and to prevent movement. The catheter tip is placed in the main bronchus of the remaining lung so that pressure on the fistula during the positive phase of the respiratory cycle is prevented. The upward stream of ventilatory gases prevents the entrance of sealant into the remaining lung. A 14-FG oxygen catheter with side holes (Airlife Inc., Monclair, CA 91763) is used for HFV.

Figure 1 shows the technique in three phases. Ventilation may be interrupted for up to 60 seconds as soon as the sealant is in place, to allow it to start drying. The sealant

adheres to the tissue and is dry after 10–12 minutes. Codeine 10 mg is given intramuscularly to prevent coughing after the treatment. Lignocaine 4% is sprayed into the larynx and trachea before extubation, and the HFV insufflation catheter is withdrawn and used as a suction catheter. Alizapride (USA) 50–100 mg is injected intravenously to prevent postoperative vomiting.

Short-acting drugs are used for general anaesthesia. Alfentanil 1 mg followed by methohexitone 1 mg/kg is used for induction, and suxamethonium 1 mg/kg administered. Intravenous anaesthesia by infusion is started immediately after induction. Two solutions are used: a hypnotic–analgesic solution that contains methohexitone 500 mg and alfentanil 5 mg in 250 ml glucose–saline administered by an infusion pump, started at 200 ml/hour for 10 minutes and then continued at 100 ml/hour; and a 0.1% suxamethonium drip infusion started at 80–100 drops/minute.

Results

Fourteen patients were treated for bronchopleural fistulae under general anaesthesia. There were 13 men and one woman, aged 52–77 years and of ASA grades 1–3. Thirteen patients had pneumonectomy for malignancies of the lung and one patient had a resection of the left upper lobe for a bronchogenic cyst. Three of the patients were treated with irradiation postoperatively. Three patients had a history of severe chronic obstructive pulmonary disease and were taking medication for it. Otherwise, pre-operative lung function tests and blood gas analysis showed no unexpected values. Fourteen patients received a total of 28 treatments. Ventilation was adjusted according to blood gas analysis and arterial oxygen saturation (SaO_2) measured by pulse oximetry. The values found immediately after sealing and a short period of apnoea during drying of the sealant (approximately 60 seconds), for 25 treatments, were pH 7.37 (range 7.23–7.50), PaCO_2 5.3 kPa (range 3.9–6.9), PaO_2 26.1 kPa (range 8.15–33.6). PaCO_2 increased to 9.6, 8.3 and 8.0 kPa respectively during three other treatments while PaO_2 was in the normal range.

Bronchopleural fistulae were sealed in four patients but in two the closure of the fistula required operation. Two patients later died from their malignancy.

Discussion

This method of ventilation and anaesthesia permits the use of both rigid and flexible bronchoscopes while only the thin insufflation catheter is passed through the glottis. The sealing is done under continuous ventilation with only a short

interval for drying of the sealant. The lungs hardly move during HFV so the operator has a good view of the working area.

Aluminium foil seems at present to be the best material to stiffen the insufflation catheter and thus to prevent its movement with every insufflation during HFV. The foil has to be fixed firmly on to the insufflation catheter, otherwise it may come off the catheter and be pushed into the bronchus. A flexible, thin metal insufflation catheter may be available soon and would prevent this risk.

The use of HFV also permits ventilation of the remaining lung without pressure of ventilatory gases on the fistula. This is of particular importance during the application of the sealant and the drying period.

The use of short-acting drugs for intravenous anaesthesia allows rapid recovery. The surgical treatment succeeds in about 20% of patients and the success rate seems to depend on how long the fistula has been present. More than one treatment is usually needed to achieve closure of a bronchial stump fistula.

References

1. JESSEN C, SHARMA P. Use of fibrin glue in thoracic surgery. *Annals of Thoracic Surgery* 1985; **39**: 521–4.
2. KRAM HB, SHOEMAKER WC, HINO ST, CHIANG HS, HARLEY DP, FLEMING AW. Tracheal repair with fibrin glue. *Journal of Thoracic and Cardiovascular Surgery* 1985; **90**: 771–5.
3. WACLAWICZEK HW, CHMELIZEK F. Endoscopic treatment of bronchus stump fistulae following pneumonectomy with fibrin sealant in domestic pigs. *Thoracic and Cardiovascular Surgeon* 1985; **33**: 344–6.
4. HAAS S, STEMBERGER A, DUSPIVA W, WEIDRINGER JW, IPPSICH A, BLÜMEL G. In: SCHEELE J, ed. *Fibrin Klebung*. Berlin: Springer Verlag, 1984: 6–10.
5. REDL H, SCHLAG G, DINGES HP. Methods of fibrin seal application. *Thoracic and Cardiovascular Surgeon* 1982; **30**: 223–7.
6. THETTER O. Fibrin adhesive and its application in thoracic surgery. *Thoracic and Cardiovascular Surgeon* 1981; **29**: 290–2.
7. EL-BAZ N, EL-GANZOURI A, GOTTSCHALK W, JENSIK R. One-lung high-frequency positive pressure ventilation for sleeve pneumonectomy: an alternative technique. *Anesthesia and Analgesia* 1981; **60**: 683–6.
8. SCHECK PA, MALLIOS C. Peroral endoscopies using intravenous anesthesia and high-frequency ventilation. *Critical Care Medicine* 1984; **12**: 803–5.
9. SCHECK PA, MALLIOS C, KNEGT P, VAN DER SCHANS EJ. High frequency ventilation in laser surgery of the larynx. *Clinical Otolaryngology* 1984; **9**: 203–7.
10. KATZ RL, BERCI G. The optical stylet—a new intubation technique for adults and children with specific reference to teaching. *Anesthesiology* 1979; **51**: 251–4.

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Teaching guided fibreoptic nasotracheal intubation

An assessment of an anaesthetic technique to aid training

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Summary

An anaesthetic technique suitable for training in fibreoptic intubation is described. It uses a capped oropharyngeal airway which leaves the nose free for fibreoptic intubation and allows the airway to be maintained and ventilation to be controlled if necessary.

An assessment is made of the technique after 50 fiberoptic intubations with the Olympus LF-1 fibroscope. There were no failed intubations and no serious complications.

Key words

Equipment; intubating fibroscope.

Intubation, tracheal; technique, training.

The use of fiberoptic endoscopes to aid intubation was first described in 1967 by Murphy¹ who used a choledochoscope for guided nasotracheal intubation. Taylor and Towey² in 1972 described the use of a bronchofibroscope as an aid to nasotracheal intubation. Subsequent papers described the use of fibroscopes to aid intubation in difficult situations.³⁻⁵ The range of instruments first used included gastroscopes and bronchofibroscopes. A first generation of purpose-designed intubating fibroscopes appeared subsequently.⁶⁻⁸

Improved designs such as the Olympus LF1 used in our hospital, have become available in the light of the experience gained with these fibroscopes. Nevertheless, the number of anaesthetists trained in fiberoptic intubation is probably small. The purpose of this study was to devise and evaluate an anaesthetic technique that provided suitable conditions to train anaesthetists in this method of intubation.

Method

Fifty patients aged 15-30 years (males) and 16-40 years (females), of ASA grade 1 or 2, scheduled to undergo elective oral surgery that required nasotracheal intubation were selected. A pre-operative assessment was made of the expected difficulty of intubation. The patients were pre-medicated with papaveretum and hyoscine. Two anaesthetists were required, one to supervise the anaesthetic and instruct, the other to perform the intubation. Anaesthesia was induced with a sleep dose of thiopentone after the start of ECG monitoring. Diazemuls 0.1 mg/kg was also used in some patients. The patients breathed halothane, nitrous oxide and 33% oxygen spontaneously until surgical anaesthesia was reached and then halothane in oxygen only. Cocaine 5% 1 ml was instilled into each nostril as a vasoconstrictor; this dose is within the recommended maximum dose of 1.5-3.0 mg/kg up to 200 mg.⁹ A Guedel oropharyngeal airway with a Nosworthy chimney (Portex Ltd, Fig. 1)* was then inserted and tape applied over the



Fig. 1. Guedel oropharyngeal airway with Nosworthy chimney.*

flange to the face to make a gas-tight seal. Anaesthesia was maintained via a Nosworthy catheter mount attached to the anaesthetic breathing system. The gas-tight seal around the mouth allows assisted ventilation if required and leaves the nose free for fiberoptic intubation (Fig. 2). An appropriately sized cuffed nasotracheal tube (7.0 mm internal diameter for males, 6.0 mm for females) with a plastic Cobb connector (Portex), was well coated with lubricant jelly and inserted

* The Guedel airway with a Nosworthy chimney is no longer produced by Portex Ltd, but has been replaced by a similar airway with a standard 15-mm connector.



Fig. 2. Modified Guedel airway and Nosworthy catheter mount.

over the fibroscope (Olympus LF1, Keymed Ltd) until held by the taper at the proximal end.

The fibroscope was held close to the patient's head to estimate the length of scope required to reach the larynx, and then inserted into the more patent nostril. The time taken from insertion into the nose to visualisation of the larynx was recorded. Ease of visualisation of the larynx was graded as follows (after Ovassapian *et al.*¹⁰): not difficult, the fibroscope was already aligned for a good view of the vocal cords on initial introduction, so that little or no manipulation of the tip of the scope was needed; moderately difficult, moderate manipulation of the fibroscope in all directions was necessary to locate the vocal cords; difficult, extensive manipulation of the fibroscope, often with changes in position of the operator, was necessary to locate the vocal cords.

Any difficulties such as fogging of the lens, bleeding, secretions and the need for the fibroscope to be withdrawn for the lens to be cleaned or antifogging agent to be applied, were recorded together with the use of suction. Suxamethonium 1 mg/kg was administered after the larynx was visualised. The fibroscope was then advanced into the larynx as far as the carina and the tracheal tube railroaded over the fibroscope into the trachea. Manual ventilation with 100% oxygen via the chimney airway was possible if the intubation was not performed immediately. The number of attempts required to railroad the tracheal tube was recorded as well as any failure, or displacement into the oesophagus. The fibroscope was withdrawn when the tracheal tube had negotiated the larynx, and a visual check made that the tracheal tube was still in the trachea. The suction cap of the Cobb connector was closed and the patient connected to the anaesthetic breathing system. The intubation was considered to be complete at this point and the total intubation time was recorded.

Direct laryngoscopy was performed with a Macintosh laryngoscope after the capped oropharyngeal airway was removed. The intubation was graded according to the method of Cormack and Lehane.¹¹

Any trauma to the nose or pharynx was noted. The patients were seen postoperatively to assess the incidence of sore nose and throat, and trauma to the mouth and lips. The supervising anaesthetist in this trial (R.T.) had considerable experience of fiberoptic nasotracheal intubation. The two operators were relative novices with this technique.

Table 1. Intubation grading.

	Grade			
	1	2	3	4
Number of cases	41	5	2	2
Percentage of total	82	10	4	4
Mean (SD) time to locate, seconds	42.27 (46.83)	31.4 (17.91)	36.5 (4.95)	428.5 (539.5)
Mean (SD) intubation time, seconds	135.07 (62.05)	113.6 (32.9)	126.5 (2.12)	520 (494.97)

Table 2. Technical difficulties.

Lens fogging	18%
Withdrawal for application of antifogging agent	4%
Epistaxis	22%
Withdrawal of instrument for cleaning	4%
Secretions	22%
Failure to clear by suction facility	0%
Passage through nose difficult	10%
Passage through nose impossible	0%

Results

The anaesthetic provided suitable conditions for unhurried endoscopy in all patients except one. A clear airway was maintained by the Nosworthy chimney oropharyngeal airway and firm chin elevation provided by the supervising anaesthetist. The supervising anaesthetist was able to ventilate the patient's lungs, after suxamethonium was administered, via the Nosworthy chimney airway during and after intubation until the cuff was inflated on the tracheal tube. The amount of gas lost through the patient's nose was compensated by an increase of the fresh gas flow to the anaesthetic breathing system. There was no failed intubations with the fibrescope in the 50 patients studied.

Intubation times. The mean time to see the larynx in 49 cases was 41.02 seconds (SD 43.21). The mean time to complete intubation in 49 cases was 132.63 seconds (SD 58.31).

Visualisation of the larynx. Visualisation of the larynx was assessed to be not difficult in 30%; moderately difficult in 64%; and difficult in 6% of patients. The grade of laryngoscopy, the time taken to locate the larynx and the mean intubation time are shown in Table 1. The technical difficulties associated with use of the instrument are shown in Table 2.

The tube was easily railroaded on 54% of occasions, whereas on 14% more than five attempts were required; the remainder needed between two and five attempts. There were no cases of failure to achieve railroading and no oesophageal intubations. Forty percent of patients complained of a sore throat postoperatively and 2% of a sore nose. There were no instances of trauma to the lips, mouth or teeth. There was one case of transient aphonia that lasted 12 hours. The fiberoptic intubation was straightforward in this case and the tracheal tube passed at the first attempt. The aphonia resolved spontaneously.

Discussion

Blind nasal intubation (BNI) has a success rate of 85.6–97.1% in the management of difficult intubation in experienced hands.^{12–15} Fiberoptic nasal intubation (FNI) has a higher success rate^{7,10,16,17} in comparison but it involves more preparation of equipment. It can be expected to be less traumatic than BNI since direct vision is used. Modern fibrescopes designed specifically for guided tracheal intubation are now available; the Olympus LF-I used in our hospital is a recent example. The insertion tube has a working length of 600 mm and an outer diameter of only 4 mm. The optical

system is forward looking, has a field of view of 75° and a depth of field of 3–50 mm. The flexible end section has an outer diameter of 3.8 mm and can be directed through an arc of 240° by means of the directional control. A third channel has an internal diameter of 1.2 mm and can be used for suction, to instill local anaesthetic solutions or to pass guide wires.¹⁸ The insertion tube is flexible until it is pulled taut when it becomes stiff and allows manipulation in an axial direction. The demand for learning this method will probably increase because of the availability of fibrescopes like this, with improved optical systems compared to earlier models,^{6–8} and given the high success rate of the technique.

The technique may appear to be easy in experienced hands but an inexperienced operator is likely to fail with a difficult intubation. One authority has recommended a minimum of 30 successfully performed intubations on normal patients before the operator is ready to attempt a difficult intubation.¹⁹ The problems commonly encountered are loss of orientation which results in impaction in the pharynx and a 'red-out', excessive secretions and bleeding.^{20,21} Reduction of tongue tonus during general anaesthesia leads to a reduction in the supraglottic space and the scope contacts the mucosa which also results in a 'red-out'. Oral intubation is more difficult than nasal because of the acute angulation with which the fibrescope must enter the larynx. Both will fail if the tracheal tube cannot be railroaded into the trachea.

We found that location of the larynx was not difficult in 30% of patients. Insertion of the fibrescope in these patients resulted in immediate approximation of the cords in a similar fashion to blind nasal intubation. Some manipulation of the fibrescope was required to direct it into the larynx in the majority of patients (64%). Extensive manipulation of the fibrescope was required in a small number (6%). Eighty-two percent of the patients were grade 1, 10% were grade 2, 4% were grade 3 and 4% were grade 4 in difficulty when direct rigid laryngoscopy (DRL) was performed. The numbers in groups 2, 3 and 4 were, as expected, small. We found, as others¹⁰ have suggested, that the difficulty of direct rigid laryngoscopy does not always correspond to difficulty of FNI.

We found that in FNI, like BNI, passage of the tracheal tube through the larynx can be difficult, possibly because the bevel of the tube catches on the arytenoids. We have found rotation of the tube, change of the axis of the airway and external laryngeal manipulation to be helpful to produce disimpaction, as with classical BNI. The use of a plastic Cobb connector in addition allows orientation of the tube so as to split the cords with the bevel of the tube.

The two grade 4 intubations in this series deserve amplification. The first was an 18-year-old girl with Still's disease, a hypoplastic mandible, a small, receding chin and degenerative changes in her cervical spine and temporomandibular joints. She was anaesthetised in the standard manner but her airway became difficult to maintain as she lost tongue tonus. Insertion of the oropharyngeal airway only partly relieved this and fiberoptic laryngoscopy became difficult as the air space between her tongue and posterior pharyngeal wall became obliterated. The operator could not see the larynx because of a persistent 'red-out'. The operator was relieved after 10 minutes by the senior

anaesthetist who experienced the same difficulty but located the larynx in 3.5 minutes and completed the intubation in 4.5 minutes. It was concluded that she would be better managed in the future by an awake intubation. We excluded her results from the trainee operators' time statistics because of the changeover of operators. The second grade 4 intubation was a 30-year-old man with osteomyelitis of the mandible. His mouth opening pre-operatively was limited to 4 mm. He was anaesthetised in the standard manner. The trismus relaxed sufficiently to insert a small chimney airway and FNI was uneventful.

The ease of FNI does not always correspond with that of DRI so training on routine uncomplicated oral surgery patients who require nasotracheal intubation may provide valuable experience for difficult intubations. The anaesthetic technique we have described allows adequate time for the novice to be taught fibreoptic intubation under ideal conditions of anaesthesia, without intermittent interruption for ventilation of the patient via a face mask. Spontaneous ventilation with inhalational anaesthesia corresponds most closely to the situation that occurs during an awake FNI although of course some degree of loss of tongue tone is inevitable, which can be compensated for by firm mandibular and if necessary sub-mandibular pressure.

The anaesthetic technique we have described, of spontaneous ventilation with halothane, may not be suitable for elderly or sick patients. The capped airway allows controlled ventilation in these patients and we have performed guided fibreoptic intubation successfully with this alternative anaesthetic technique.

In conclusion fibreoptic intubation in skilled hands provides the highest success rate during difficult intubations. It is important that experience is gained on normal subjects before a predicted difficult intubation is attempted. We hope that the demand for the use and hence the teaching of fibre-optic intubation will increase in all hospitals.

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References

- MURPHY P. A fibre-optic endoscope used for nasal intubation. *Anaesthesia* 1967; **22**: 489-91.
- TAYLOR PA, TOWEY RM. The broncho-fibrescope as an aid to endotracheal intubation. *British Journal of Anaesthesia* 1972; **44**: 611-2.
- HAINS JD, GIBBIN KP. Fibreoptic laryngoscopy in ankylosing spondylitis. *Journal of Laryngology and Otology* 1973; **87**: 699-703.
- EDENS ET, SIA RL. Flexible fiberoptic endoscopy in difficult intubations. *Annals of Otology, Rhinology and Laryngology* 1981; **90**: 307-9.
- SINCLAIR JR, MASON RA. Ankylosing spondylitis. The case for awake intubation. *Anaesthesia* 1984; **39**: 3-11.
- DAVIES NJ. A new fiberoptic laryngoscope for nasal intubation. *Anesthesia and Analgesia* 1973; **52**: 807-8.
- STILES CM, STILES QR, DENSON JS. A flexible fiber-optic laryngoscope. *Journal of the American Medical Association* 1972; **221**: 1246-7.
- RAJ PP, FORESTNER J, WATSON TD, MORRIS RE, JENKINS MT. Technics for fiberoptic laryngoscopy in anaesthesia. *Anesthesia and Analgesia* 1974; **53**: 708-13.
- COE PA, KING TA, TOWEY RM. Toxic dose of cocaine and adrenaline. *Today's Anaesthetist* 1987; **2**: 32.
- OVASSAPIAN A, YELICH SJ, DYKES MHM, BRUNNER EE. Fiberoptic nasotracheal intubation—incidence and causes of failure. *Anesthesia and Analgesia* 1983; **62**: 692-5.
- CORMACK RS, LEHANE J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39**: 1105-11.
- GILLESPIE NA. Blind nasotracheal intubation. *Anesthesia and Analgesia* 1950; **29**: 217-22.
- GOLD MI, BUECHEL DR. A method of blind nasal intubation for the conscious patient. *Anesthesia and Analgesia* 1960; **39**: 257-63.
- DEFALQUE RJ. Ketamine for blind nasal intubation. *Anesthesia and Analgesia* 1971; **50**: 984-6.
- OYEGUNLE AO. The use of Propanidid for blind nasotracheal intubation. *British Journal of Anaesthesia* 1975; **47**: 379-81.
- MESSETER KH, PETTERSSON KI. Endotracheal intubation with the fibre-optic bronchoscope. *Anaesthesia* 1980; **35**: 294-8.
- KEENAN MA, STILES CM, KAUFMAN RL. Acquired laryngeal deviation associated with cervical spine disease in erosive polyarticular arthritis. Use of the fibreoptic bronchoscope in rheumatoid disease. *Anesthesiology* 1983; **58**: 441-9.
- STILES CM. A flexible fibreoptic bronchoscope for endotracheal intubation of infants. *Anesthesia and Analgesia* 1974; **53**: 1017-9.
- SIA RL, EDENS ET. How to avoid problems when using the fibre-optic bronchoscope for difficult intubations. *Anaesthesia* 1981; **36**: 74-5.
- LLOYD E LI. Fibreoptic laryngoscopy for difficult intubation. *Anaesthesia* 1980; **35**: 719.
- ANDERTON JM. Difficulty in intubation. *British Journal of Anaesthesia* 1978; **50**: 1267.

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Urea and electrolyte measurement in pre-operative surgical patients

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Summary

In a prospective study of 1062 patients who presented for routine and emergency surgical procedures, the frequency of urea and electrolyte measurement was determined. In addition, the incidence of abnormal urea and electrolyte measurements were recorded. It was found that these abnormal values were most frequent in the paediatric population (though they had the fewest urea

and electrolyte measurements performed) and in the over 60s. The American Society of Anesthesiologists' grade was found to be a useful predictor as to whether the urea and electrolyte measurement could be expected to be abnormal. It is suggested that American Society of Anesthesiologists' Grade I patients do not require routine urea and electrolyte measurements whilst those in grades 3, 4 and 5 and those on diuretics do.

Key words

Fluid balance; electrolytes.

Urea and electrolyte measurement is a frequently but inconsistently performed investigation in both the elective and emergency surgical patient. It is of particular interest to the anaesthetist because an abnormal urea and electrolyte result may influence the anaesthetist in his/her choice of anaesthetic technique and, indeed, the anaesthetic agents may themselves cause changes in electrolyte levels which may be of clinical significance (for instance potassium with suxamethonium^{1,2} and sodium with thiopentone).³

This study was designed to indicate in which patients a urea and electrolyte estimation should be requested and in which patients such a request would be unlikely to produce abnormal results. None of the standard anaesthetic text books advise when this investigation is and is not appropriate.

Method

The records of 1062 patients were analysed prior to anaesthesia and they were allocated to the appropriate American Society of Anesthesiologists' grade (ASA) after examination both of the patients themselves and of their records. Note was taken of the patient's age, ASA grade, the presence or absence of a urea and electrolyte result and, if present, whether this investigation was normal or abnormal.

Table 1. Normal urea and electrolyte values.

	(mmol/litre)
Na ⁺	135-145
K ⁺	3.5-5.5
Cl ⁻	95-110
Urea	2.5-7.5

A urea and electrolyte result was considered abnormal if it deviated from the normal reference range used in this hospital (Table 1).

Results

The records of 1062 patients were analysed. The patients had presented for minor and major surgery in the six specialties located at this hospital in an elective and emergency setting. The number of patients from each specialty represents the author's exposure to these specialties over a 4-month period.

The percentage of patients with urea and electrolyte estimations ranged from 6% in the obstetric and gynaecology patients to 85% in the orthopaedic patients. Similarly, the percentage of those with abnormal urea and electrolyte, ranged widely from 0% in the obstetric and gynaecology patients to 37% in the orthopaedic population studied (Table 2).

When the patients' ages were taken into account approximately 25% of those under 50 had had urea and electrolyte measurements performed; in the over 50s this fraction increased to over 80%. There was a peak in the under 20s of abnormal urea and electrolytes in those patients in whom urea and electrolyte measurements were performed. This peak declined until the 30s when again the percentage of those with abnormal urea and electrolytes gradually increased, to almost 50% in the over 80s. There were insufficient patients in the over 90s to subdivide this group further (Table 3).

Both in elective and emergency patients, with ASA grades in mind, there is a gradual increase in the percentage of abnormal urea and electrolytes from just over 1% in

Table 2. Normal/abnormal urea and electrolyte according to speciality.

Speciality	Number of patients	Percent with urea and electrolyte	Percent with abnormal urea and electrolyte
Obstetrics/gynaecology	279	6	0
Maxillofacial	51	37	11
Orthopaedics	257	85	37
Plastics	170	59	19
Paediatrics	133	12	6
General surgery	172	84	14

Table 3. Patients with urea and electrolyte and abnormal urea and electrolyte according to age.

Age	Number of patients	Percent with urea and electrolyte	Percent with abnormal* urea and electrolyte
0-10	114	8	11
11-20	103	29	10
21-30	173	25	2
31-40	146	22	0
41-50	90	29	15
51-60	91	77	11
61-70	94	84	19
71-80	151	88	33
over 80	100	97	49
Total	1062	49	24

* $\frac{\text{Abnormal urea and electrolyte}}{\text{Total with urea and electrolyte}} \times 100$

Table 4. Percentage with abnormal urea and electrolyte according to American Society of Anesthesiologists' grade.

ASA Grade	Routine, % abnormal	Emergency % abnormal	Total, % abnormal
1	2	0	1.5
2	16	19	17
3	37	28	35
4 and 5	55	37	48

Table 5. Urea and electrolyte in patients taking diuretics.

Number with urea and electrolyte	Percent abnormal
67	48

Table 6. Urea and electrolytes in vomiting patients.

Number with urea and electrolyte	Percent abnormal
19	16

grade 1 patients to 48% in grade 4 and 5 patients. There were too few patients in grade 5 to warrant further subdivision (Table 4).

Diuretics were taken by 67 patients with urea and electrolyte measurement available and of these 48% were abnormal (Table 5). Nineteen patients were vomiting and had a urea and electrolyte measurement, 16% of which were abnormal (Table 6).

Discussion

There has been a debate over the usefulness of routine pre-operative laboratory investigation. For example Kaplan *et al.*⁴ reported that approximately 60% of these pre-operative tests were not indicated. It seems that the emphasis has been placed on the avoidance of unnecessary testing.⁵⁻⁷ This study confirms that urea and electrolytes are needlessly performed in some, but also that it is not carried out in others in whom an abnormal result is more probable. A recent study by McKee and Scott⁸ has shown that urea and electrolyte measurement should be carried out in the over 60s. In this study, of the 345 patients over 60 years of age, 36 had no urea and electrolyte estimation performed. Indeed three patients over the age of 80 arrived to theatre without a urea and electrolyte measurement, when the results of this investigation show that almost 50% of this group could be expected to have had abnormal and possibly significant abnormalities.

Similarly, this study demonstrates that chronological age alone is not necessarily the best indication to perform the investigation. Of the 216 patients with urea and electrolyte below the age of 60, 16 were abnormal. Age alone gives no indication of physical health. The ASA grade, however, is determined by the patient's health and the figures indicate that it is a relatively accurate method to determine urea and electrolytes. In ASA grade 1 patients only 1.5% were found to have abnormal results. Of these patients one had a urea of 7.9 mmol/litre which though outside the reference range of this hospital would have been inside that of others. The other patient had a K⁺ of 2.9 mmol/litre which was unexpected and unexplained. Conversely, almost 50% of

the grade 4 and 5 patients had abnormal tests. Seventeen percent of grade 2 patients had abnormal urea and electrolytes and therefore the decision to perform this test may be influenced by the nature of the operation and anaesthetic technique and whether baseline values would be beneficial in the guidance of postoperative care.

Almost 50% of those taking diuretics had abnormal urea and electrolytes, and therefore the use of these drugs by the patient should be an indication for a urea and electrolyte test. Interestingly less than one in five of those vomiting had abnormalities in their urea and electrolytes.

The high incidence of abnormalities in the urea and electrolytes of the orthopaedic, and to a lesser extent, the plastic surgery population studied probably reflects the more advanced age of this population, and consequently poorer health and higher ASA grade. The absence of abnormal urea and electrolytes in the obstetric and gynaecology patients presumably does not represent exemplary health in this group (as many of them were elderly) but rather inadequate criteria for selection for urea and electrolyte testing.

No attempt has been made in this study to decide whether an abnormality in the urea and electrolyte would alter the technique used by the anaesthetist. Consequently, many of the abnormal urea and electrolytes recorded would not in themselves have influenced the technique used, but when taken with the patient's state as a whole may have caused alterations.

In summary, the results of this study suggest that the anaesthetist should request a urea and electrolyte measurement in any ASA grade 3 to 5 patient, and possibly in grade 2 patients depending on the nature of the surgery and anaesthetic technique proposed. There seems to be no need to perform a urea and electrolyte test on ASA grade 1 patients. Diuretic use is also an indication for urea and electrolyte estimations.

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I would like to thank Ms S. Lyle Hall for her help in typing this manuscript.

References

1. WEINTRAUB HD, HEISTERKAMP DV, COOPERMAN LH. Changes in plasma potassium concentration after deploring blockers in anaesthetised man. *British Journal of Anaesthesia* 1969; **41**: 1048-52.
2. COLLIER CB. Suxamethonium pains and early electrolyte changes. *Anaesthesia* 1978; **33**: 454-61.
3. BALI IM, DUNDEE JW. Immediate changes in plasma potassium, sodium and chloride induced by intravenous induction agents. *British Journal of Anaesthesia* 1974; **46**: 929-33.
4. KAPLAN EB, SHEINER LB, BOECKMANN AJ, ROIZEN MF, BEAL SL, COHEN SN, NICOLL CD. The usefulness of preoperative laboratory screening. *Journal of the American Medical Association* 1985; **253**: 3576-81.
5. Routine preoperative investigations are expensive and unnecessary. LEADING ARTICLE, *Lancet* 1983; **2**: 1466-67.
6. DURBRIDGE TC, EDWARDS F, EDWARDS RG, ATKINSON M. Evaluation of benefits of screening tests done immediately on admission to hospital. *Clinical Chemistry* 1976; **22**: 968-71.
7. LUNDBERG GD. Is there a need for routine preoperative laboratory tests? *Journal of the American Medical Association* 1985; **253**: 3589.
8. MCKEE RF, SCOTT EM. The value of routine preoperative investigations. *Annals of the Royal College of Surgeons of England* 1987; **69**: 160-2.

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Radiotherapy and children's anaesthesia

Paediatric patients who require sedation for radiotherapy treatments in our hospital are usually given either an inhalational anaesthetic or intramuscular ketamine. Methohexitone is an established intravenous induction agent and has been used via the intramuscular route in children who require electroencephalography and CT scanning.^{1,2} We found that methohexitone produces suitable sedation for the treatment period with improved recovery criteria one hour after administration in a pilot study which compared intramuscular ketamine and methohexitone during selected radiotherapy procedures.

Consecutive patients who required anaesthesia for radiotherapy were entered into the trial after their parents' informed consent was obtained. However, children were excluded from the trial if their treatment involved any potentially painful or uncomfortable procedures. Patients were fasted and received oral premedication 2 hours before treatment of trimeprazine syrup (3 mg/kg) and atropine (0.02 mg/kg). Each child received either methohexitone sodium (8 mg/kg as 5% solution in water) or ketamine (10 mg/kg as 10% solution) by deep intramuscular injection.

The child was then allowed to go to sleep undisturbed in a parent's arms. The time taken for the onset of satisfactory sedation and any induction difficulties were noted, and the child was then placed in position for treatment. The patient was closely monitored, once positioned, with a pulse oximeter and closed circuit television. Recovery was observed by a nurse when the treatment finished; she completed a three-point recovery score chart at 10-minute intervals, unaware of which drug the child had been given, and the next day the same procedure was followed with the alternate induction agent. The recovery score was derived from 3 criteria: awake (fully, 2; arousable, 1; unresponsive, 0) ventilation (can cough, 2; breathing regularly, 1; apnoeic, 0) and movement (spontaneous, 2; to stimulation, 1; not moving, 0).

There was no apparent difference in speed or ease of induction between the two agents, and each produced suitable sedation for treatment. However, recovery from methohexitone was found to be more rapid, more complete and free of the dreams and hallucinations characteristic of ketamine. Mean recovery scores of the six patients at 10-

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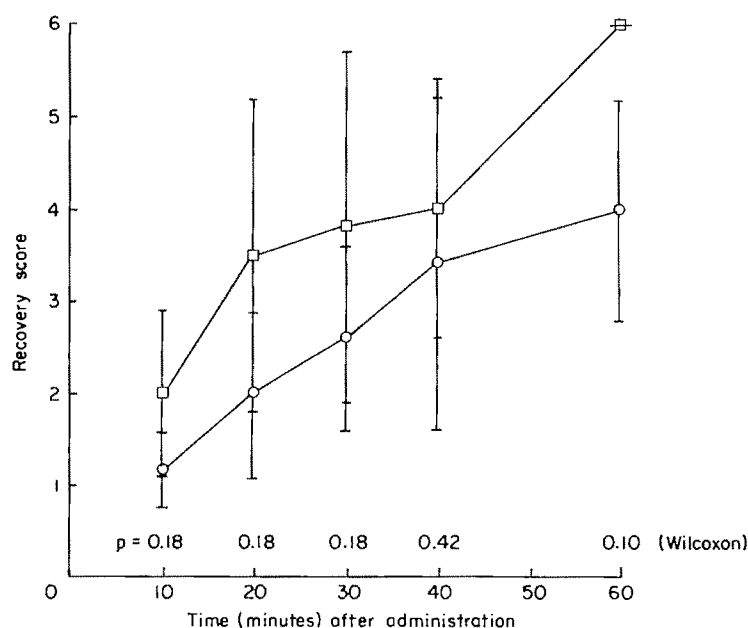


Fig. 1 Mean recovery scores and their standard deviations after administration of ketamine (O) and methohexitone (□) to six children.

minute intervals are shown (Fig. 1). Differences in scores were significant ($p = 0.01$) at the 60-minute interval but our sample was small. In three patients recovery from methohexitone was consistently better than that from ketamine. In one patient neither was superior, but in no patient was ketamine better.

We confirm that methohexitone, with premedication, is a useful intramuscular induction agent for children who have repeated treatments and require sedation; however, procedures which involve pain or undue stimulation are unsuitable for methohexitone sedation. It should only be used by an anaesthetist since there is a potential for upper airway obstruction. No difficulties were encountered with its use, and recovery was superior and more predictable. This last feature was particularly noted by the children's parents, most of whom requested further use of metho-

hexitone, and 24 more anaesthetics with this agent were performed in three of these children. The encouraging results of this pilot study require further investigation.

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References

1. FRANK GS, FRASER RAR, WHITCHER C. Intramuscular methohexitone for rapid induction of short duration sleep in the EEG laboratory: A study of forty-four hyperkinetic children. *Electroencephalography and Clinical Neurophysiology* 1966; 21: 76-8.
2. VARNER PD, EBERT JP, MCKAY RD, NAIL CS, WHITLOCK TM. Methohexitone sedation in children undergoing CT scan. *Anesthesia and Analgesia* 1985; 64: 643-5.

Career prospects in anaesthesia

A count of the numbers and types of consultant and senior registrar posts advertised in the *British Medical Journal* and the *Lancet*, offers some encouragement to trainees. This letter summarises the results from October 1986 to September 1987.

Consultant posts. One-hundred-and-seventy-five posts were advertised within the year: 137 in England, 11 in Wales, 17 in Scotland and 10 in Northern Ireland. Sixty-three posts were advertised as new, 41 to fill retirement vacancies and 71 gave no clue as to how the post arose.

In terms of specialisation the jobs included: obstetrics (24); intensive care (40); pain relief (15); supraspecialty work (23); academic appointments (6); and nothing specified (67).

The creation of new consultant posts appears to be running at a rate higher than that expected from manpower predictions.

Senior registrars. Despite the 175 vacancies for consultant posts, 87 senior registrar posts were advertised of which 11 were for lecturer posts with honorary contracts. Seventy

were in England, four in Wales, 11 in Scotland and two in Northern Ireland.

It is welcome to note the large numbers of consultant advertisements in times when career prospects appear bleak. The fact that obstetrics, intensive care and pain relief come into nearly half the job descriptions has implications for training especially at the senior registrar level.

The relatively small number of senior registrar vacancies arises from the common practice of filling more than one vacancy at a single interview. There seems to be no problem in this practice, provided the job description for all the filled posts is the same. Nevertheless, registrars who seek promotion should be aware that it occurs. Should the trend of increasing numbers of consultant advertisements continue, then the prospects for registrars and senior registrars will improve.

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J. NORMAN

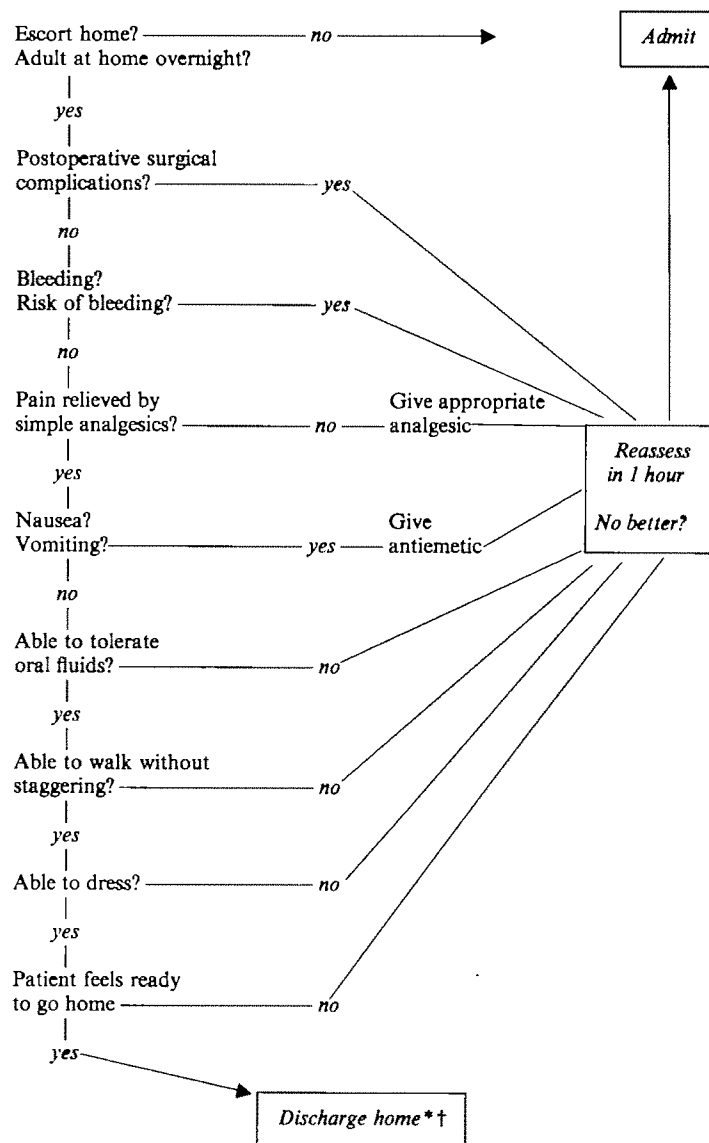
Fitness for discharge after day surgery

In our Day Surgery Unit patients are always assessed after operation by an experienced anaesthetist who consciously, or otherwise, takes into account all the factors necessary for safe discharge home; elsewhere in the hospital, however,

surgical (as opposed to anaesthetic) morbidity and the subjective ability to go home.

These guidelines may not be perfect but they are presented here to stimulate discussion of a neglected area of

Assessment of day cases for discharge



* with a supply of appropriate analgesics if necessary.

† instructions not to drive, operate machinery, cook or drink alcohol for 24 hours postoperatively.

patients may be discharged on the day of their operation by inexperienced housemen. We have had one or two complaints from these patients who considered that they were pushed out of hospital feeling unwell, and it may be assumed that there are other similar patients about whom we do not know. Some guidelines (amended from those of Korttila¹) have proved useful and popular with both nursing and medical staff.

Psychomotor tests of recovery 2 are essential for research into better day surgery techniques but are time consuming, and, more importantly, do not assess other aspects of fitness for discharge such as social factors, postoperative

anaesthetics, in view of the current enthusiasm for day surgery.

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References

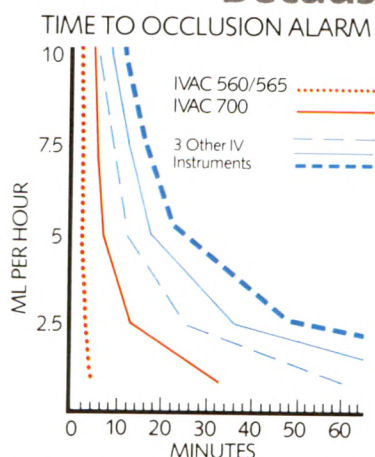
1. KORTTILA K. Full recovery after different anaesthetic techniques for short diagnostic procedures. *Acta Anaesthesiologica Belgica* 1984; 35(Suppl.): 399-411.
2. HINDMARCH I. Psychomotor function and psychoactive drugs. *British Journal of Clinical Pharmacology* 1980; 10: 189-209.

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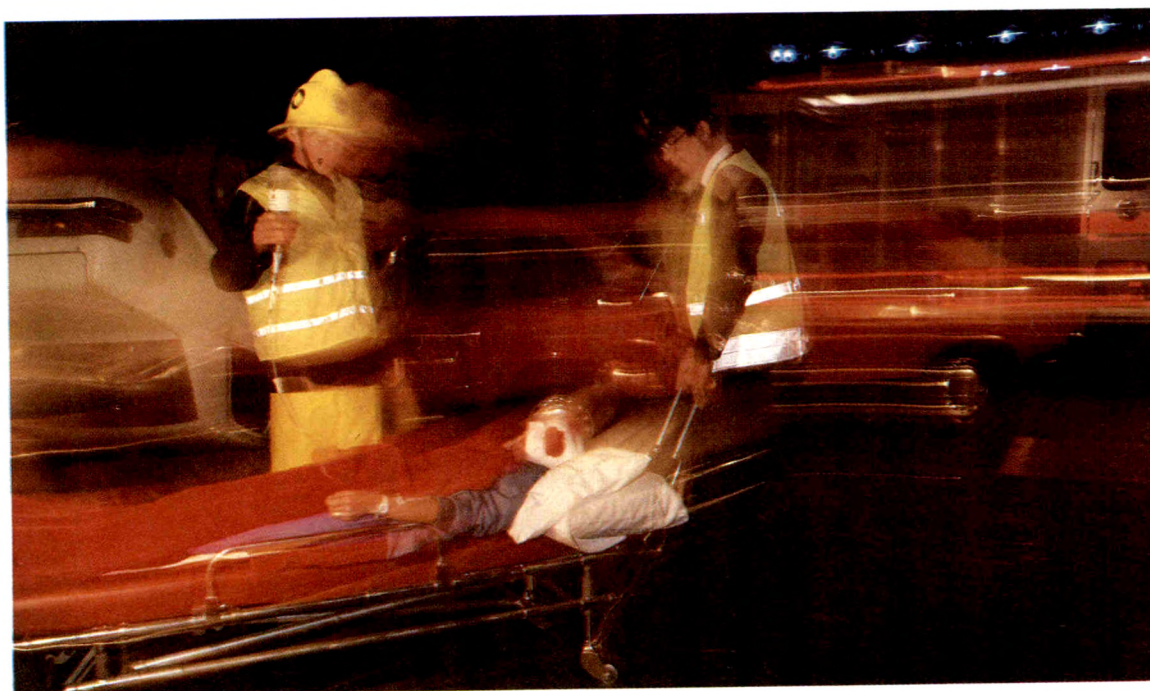
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Tracheal versus intravenous atropine

The article by Bray *et al.* (*Anaesthesia* 1987; 42: 1188–90) was interesting. They found that atropine (600 µg) given either intravenously or intratracheally in intubated anaesthetised patients produced a similar increase in heart rate, although the maximum increase occurred earlier after intratracheal administration. They conclude with the suggestion that the intratracheal route 'is the route of choice when a rapid clinical response is desired, as in an emergency'. Previous experience with intratracheal atropine during cardiopulmonary resuscitation has appeared in the form of case reports,¹ but no controlled studies have preceded the incorporation of intratracheal atropine into standard resuscitation protocols.^{2,3} Studies exist to show that atropine is adequately absorbed after intratracheal administration, and some of these have been quoted in this paper; but these are either under controlled clinical situations or in animal models.

It is interesting to consider in this context the study by Quinton *et al.*⁴ They compared plasma levels and clinical response after intravenous and tracheal adrenaline in patients who presented to an accident and emergency department with asystolic cardiac arrest. There was little or no increase in plasma adrenaline levels after tracheal administration and the clinical outcome was poor, contrary to the findings of previous reports.^{5–8} They attributed this to the presence of pulmonary oedema, atelectasis and aspiration pneumonitis. The unpredictable circulation times associated with cardiopulmonary resuscitation may also have played a part.⁹

It would seem likely that the same factors apply to atropine absorption during cardiopulmonary resuscitation. The intratracheal route may be convenient and effective in many situations, but with 'out of hospital' arrests the above factors may be important, and extrapolation of results obtained in more controlled conditions may be unwise.

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References

1. GREENBURG MI, MAYEDA DV, CHRZANOWSKI R, BRUMWELL D, BASKIN SI, ROBERTS JR. Endotracheal administration of atropine sulfate. *Annals of Emergency Medicine* 1982; 11: 546–8.
2. AMERICAN HEART ASSOCIATION. Standards and guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiac Care (ECC). Parts 3 and 4. *Journal of the American Medical Association* 1986; 255: 2933–69.
3. RESUSCITATION COUNCIL (UK). 1984 poster on cardiopulmonary resuscitation. Department of Anaesthetics, The Royal Free Hospital, Pond Street, London.
4. QUINTON DN, O'BRYNE G, AITKENHEAD AR. Comparison of endotracheal and peripheral intravenous adrenaline in cardiac arrest. Is the endotracheal route reliable? *Lancet* 1987; 1: 828–9.
5. REDDING JS, ASUNCION JS, PEARSON JW. Effective routes of drug administration during cardiac arrest. *Anesthesia and Analgesia* 1967; 46: 253–8.
6. GREENBURG MI, ROBERTS RJ, KRUSZ JC, BASKIN SI. Endotracheal epinephrine in a canine anaphylactic shock model. *Journal of the American College of Emergency Physicians* 1979; 8: 500–3.
7. ROBERTS JR, GREENBURG MI, KNAUB MA, BASKIN SI. Comparison of the pharmacological effects of epinephrine administered by the intravenous and endotracheal routes. *Journal of the American College of Emergency Physicians* 1978; 7: 260–4.
8. ROBERTS JR, GREENBURG MI, KNAUB MA, KENDRICK ZV, BASKIN SI. Blood levels following intravenous and endotracheal epinephrine administration. *Journal of the American College of Emergency Physicians* 1979; 8: 53–6.
9. KUHN GJ, WHITE CB, SWETNAM RE, MUMBY JF, RYDESKY MF, TINTINALLI JE, KROME RL, HOEHNER PJ. Peripheral vs central circulation times during CPR: a pilot study. *Annals of Emergency Medicine* 1981; 10: 417–9.

Tracheal route for emergencies?

The article of Bray, Jones and Grundy (*Anaesthesia* 1987; 42: 1188–90) was interesting. However, in the last sentence it says that the tracheal route is the route of choice when a rapid clinical response is desired, as in an emergency. The patients in the article were otherwise fit, normotensive patients under controlled anaesthesia. As reported by myself,¹ McDonald², and commented on in the recent editorial in *Anaesthesia*,³ the only controlled studies in emergencies suggest that the tracheal route cannot be relied upon for the administration of cardiac arrest.

It is important to emphasise the uncertainty of this route because clinicians may otherwise wait for a therapeutic effect rather than use a more established means of access to the circulation.

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References

1. QUINTON DN, O'BRYNE G, AITKENHEAD AR. Comparison of endotracheal and peripheral intravenous adrenaline in cardiac arrest. Is the endotracheal route reliable? *The Lancet* 1987; 1: 828–9.
2. McDONALD JL. Serum lidocaine levels during cardiopulmonary resuscitation after intravenous and endotracheal administration. *Critical Care Medicine* 1985; 13: 914–5.
3. GREENBAUM R. Editorial, Down the tube. *Anaesthesia* 1987; 42: 927–8.

Sedation with isoflurane

We wish to report the routine use of isoflurane as a sedative agent for postoperative cardiac surgical patients during controlled ventilation of the lungs in an intensive care unit. It has been our practice for 2 years to use this agent in a range of 0.5 to 1% to sedate patients, who are judged to be suitable for extubation within 6 hours of returning to the intensive care unit; this is a total exposure time to isoflurane of approximately 10 hours.

This practice has been very successful with minimal changes in cardiovascular variables. We have also used isoflurane to sedate a number of patients, mostly children,

for longer periods; some of these have received isoflurane for up to 150 hours. Monitoring of hepatorenal function has shown minimal disturbance, particularly when compared with the normal postoperative cardiac surgical patient who has received a large blood transfusion. The liver function tests have shown limited elevations of serum transaminase with return to normal within one week. Haematological indices remained normal.

Awakening after withdrawal of isoflurane is rapid and clinically the drug has proved to be a versatile, consistent and controllable agent in our patients. There is the practical

necessity to provide effective scavenging which is built-in to our intensive care unit. Analgesic requirements are based on those given during a normal anaesthetic sequence by intermittent intravenous injection. The use of isoflurane has added another drug to the armamentarium for sedation in the intensive care unit. Its physical properties and low metabolism are useful in this situation. This subject has been discussed especially since Althesin and etomidate are not available for use in these circumstances and the newer intravenous agents appear to carry similar costs to isoflurane. Other inhalational agents have been used in the intensive care unit, such as halothane¹ and even the specific occasional use of isoflurane² but the routine use of this agent in intensive care has not been previously reported.

Epidural sufentanil and intramuscular buprenorphine

Some comments are necessary about the study by Drs. Donadoni and Rolly (*Anaesthesia* 1987; **42**: 1171–5). Firstly, I question the value of a comparison of two techniques of postoperative analgesia with different drugs by different routes. There is sense in comparing the same drug by different routes, or different drugs by the same route, since conclusions can then be drawn about the pharmacokinetics or pharmacodynamics involved. This is not the case in studies such as the one by Donadoni and Rolly, which essentially compares chalk and cheese. The first choice in the provision of postoperative analgesia for any given patient is the route, and the second is which drug should be used, since the main properties of epidural or intramuscular administration are known. Studies like this one really do very little to help us make these choices.

Secondly, I question the ethical justification of inserting epidural catheters solely for the purpose of a placebo injection. The risks surrounding insertion of an epidural catheter, followed by an injection of 10 ml saline and removal of the catheter are low; nevertheless, serious complications do exist. I do not think it is justifiable to expose the patient to these risks without benefit from the epidural catheter. The validity of the trial could probably have been preserved with a fake epidural catheter in one group and by making it single-blind.

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I.G. KESTIN

Trichloroethylene

It was interesting to read the paper by Drs Rice and Reynolds (*Anaesthesia* 1987; **42**: 1320–3). As a retired anaesthetist who used trichloroethylene for some 35 years I was pleased to see that their findings offered support to my clinical impressions.

Trichloroethylene can be a very satisfactory analgesic supplement to nitrous oxide, oxygen and hyperventilation of the lungs in abdominal surgery. In the 20 or so years before 1985 I used it in this way for virtually all anaesthetics for abdominal surgery (amounting to some thousands). There was a remarkable absence of the classically attributed side-effects, waking was satisfactory and the early post-operative period was placid and relatively pain-free. Trichloroethylene 0.5% was used for an initial settling period, thereafter much lower concentrations for intermittent, brief periods (under 5 minutes) in much the same way as others might have administered a further dose of an intravenous opioid. The total dose of trichloroethylene in each case was small; indeed at Rice and Reynolds costing it

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References

1. KON H, NAMIKI A, KASHIKI K. Changes of liver function in a patient with bronchial asthma undergoing long term halothane inhalation therapy. *Hiroshima Journal of Anesthesia* 1985; **21**: 231–4.
2. BIERMAN MI, BROWN M, MUREN O, KEENAN RL, GLAUSER FL. Prolonged isoflurane anesthesia in status asthmaticus. *Critical Care Medicine* 1986; **14**: 832–3.

A reply

We thank Dr Kestin for his comments. He is certainly correct to state that our study was not a comparison of the same drug given by different routes or of different drugs by the same route. However, no information was available, at the time we planned our study, about epidural sufentanil for postoperative pain relief, except our own dose-finding report. It was our aim to evaluate clinically the usefulness of this technique in comparison with a standard conventional method of postoperative pain relief. We knew that intramuscular sufentanil has a short action, so we chose another compound with strong potency and lipophilicity—buprenorphine, which is accepted as an efficacious postoperative analgesic. We think that clinically it is useful to compare two treatment techniques, particularly in the case of the epidural administration of opioids, where a clear benefit must be present before it can be recommended for routine use. Clinical studies, together with pharmacokinetic and pharmacodynamic studies, can also improve quality, care and help decision making.

We refer to the Methods paragraph in our study: epidural anaesthesia was used as the preoperative anaesthetic technique; when lignocaine is used for orthopaedic surgery in our hospital, a catheter is always introduced to allow eventual administration of top-up doses, in case the operation is unexpectedly prolonged.

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R. DONADONI

can only have been extremely rarely that I spent as much as 2p a case.

In contrast, there seems little place for trichloroethylene with spontaneous ventilation except for short cases when other agents such as halothane and enflurane are contraindicated. In such rare circumstances, however, very small doses of intravenous opioids appear to reduce most of the disadvantages.

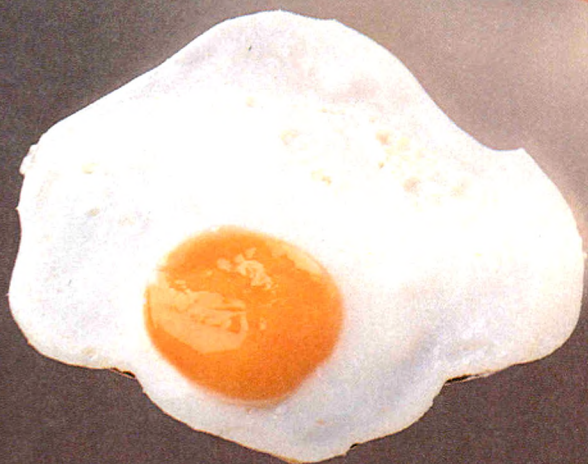
In short, the usefulness of trichloroethylene depends on the rationale behind its use. If the rationale is good (as an analgesic supplement to nitrous oxide and hyperventilation, as above) it can be very, very good, but if the rationale is bad (as an old-fashioned, 'powerful' anaesthetic) it can be horrid.

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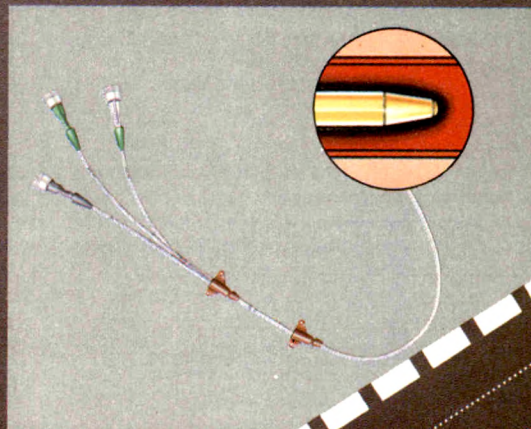
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Contents Preface ● Landmarks in the Development of Regional Analgesia [Yes, even some history] ● Anatomy and Physiology of Epidural Block ● Epidural Anaesthesia for Caesarean Section ● Analgesia in Labour ● Complication and Side-Effects of Obstetric Epidural Block ● General Anaesthesia for Caesarean Section ● Spinal Analgesia in Obstetrics ● The Physiology of Pregnancy and Anaesthesia ● Placental Transfer ● Shock in Obstetric Patients ● Pregnancy and Heart Disease ● Haemostasis in Pregnancy ● Aspiration Pneumonitis ● Management of Labour ● Pre-eclampsia and Other Conditions of Concern to the Anaesthetist ● Maternal Mortality and Anaesthesia ● Fetal Wellbeing ● Neonatal Intensive Care ● Analgesics and the Newborn Baby ● Index.

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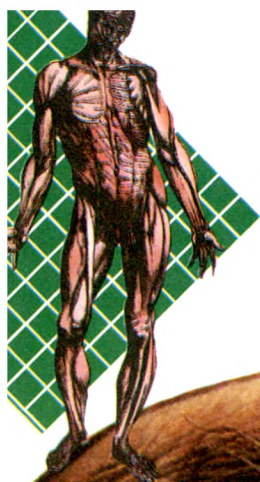
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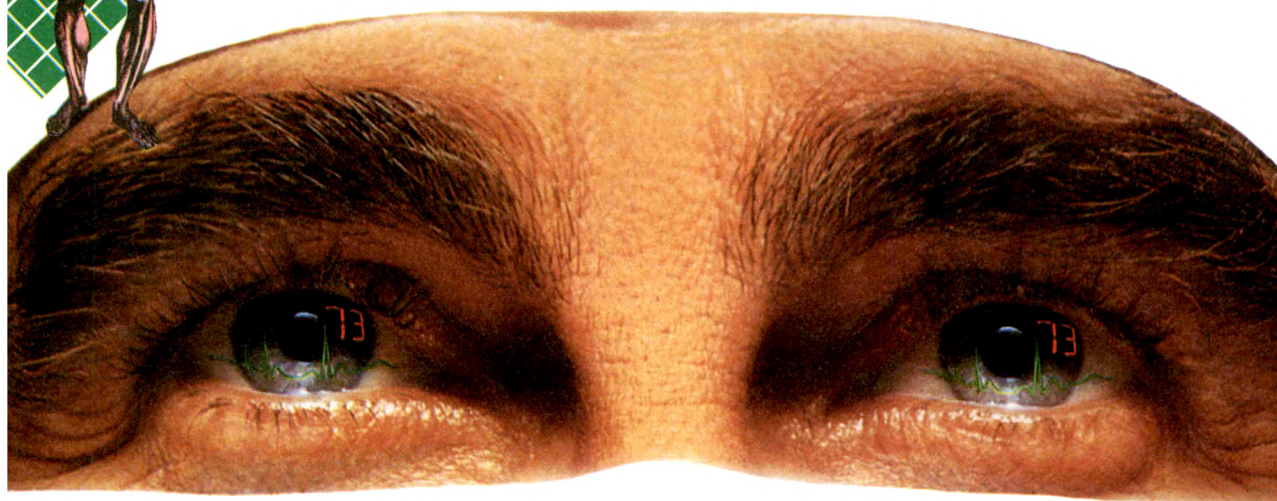


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Nasotracheal intubation

The use of nasotracheal intubation for general anaesthesia is common practice for otolaryngology lists. This appears, in some instances, to be a traumatic business which requires several attempts and often results in frank bleeding from the nose. More significantly it may include septal dislocation, turbinate avulsion and obstructive adhesion formation.^{1,2} Our experience of nasal surgery in general indicates that trauma, especially to both the septum and lateral wall of the nasal cavity, may result in nasal adhesions; a recent study has shown the incidence of nasal adhesions after such surgery is approximately 11%.³

A prospective pilot study of 36 adults who had nasotracheal intubation for routine tonsillectomy was carried out. Rhinoscopy was performed pre-operatively and 6 weeks postoperatively and the findings were recorded, with intubation details such as the size of tube and side used. The degree of difficulty encountered was also noted as well as any bleeding produced.

Of the 36 cases, 15 were considered traumatic intubations

and many of these had nasal bleeding as a result. Three intubations by this route had to be abandoned. Despite this, there were no nasal adhesions found at follow up.

We conclude that, although nasal tracheal intubation can be traumatic, it does not constitute a significant risk with regard to nasal adhesion formation.

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References

1. ATKINSON RS, RUSHMAN GB, ALFRED-LEE J. *Tracheal intubation. A synopsis of anaesthesia*. 10th edn. London: Wright; 1987: 203-220.
2. STOELTING RK. Endotracheal intubation. In: MILLER RD, ed. *Anaesthesia*. 2nd edn. New York: Churchill Livingstone, 1986: 537-8.
3. SHONE GR, CLEGG RT. Nasal adhesions. *Journal of Laryngology and Otology* 1987; **101**: 555-7.

Sinus arrest and beta blockade

We wish to report the occurrence of an uncommon cause of sinus arrest during cardiac surgery.

The patient, a 56-year-old smoker, presented with a history of increasing exertional angina poorly controlled with sublingual nitrates and metoprolol, 100 mg/day. There was no history of myocardial infarction and no other significant medical history of note. Angiography revealed triple-vessel disease, and he was scheduled for elective coronary artery vein graft surgery.

B-blockade was continued up to and including the day of operation. Premedication was with temazepam 30 mg and transdermal nitrate patch 2 hours, and morphine 15 mg one hour before operation. The patient was well sedated before induction but easily rousable, with pulse rate of 55 beats/minute sinus rhythm, and arterial blood pressure of 115/65 mmHg. Induction with fentanyl 500 µg, and midazolam 15 mg was followed by alcuronium 25 mg to facilitate tracheal intubation and controlled ventilation of the lungs. Anaesthesia was maintained with 1-3% enflurane in oxygen for approximately one hour during preparation and initial saphenous vein dissection. The heart rate remained stable, at 50-55 beats/minute sinus rhythm, and the systolic blood pressure of 95-110 mmHg. The heart rate declined sharply to asystole, immediately after median sternotomy was carried out by airpowered saw. Internal cardiac massage was performed for 30-40 seconds, while atropine, 0.8 mg was administered through the central venous line. Sinus rhythm resumed rapidly and settled

at a rate of 85 beats/minute. The operation continued uneventfully and the postoperative recovery was unremarkable.

Sudden profound bradycardia or sinus arrest is well documented in association with various well known stimuli, such as extra-ocular or peritoneal traction, rectal, urethral, or cervical dilatation, glottic or bronchial irritation and carotid sinus manipulation.¹ Much published work suggests that this phenomenon is particularly likely when vecuronium or atracurium are chosen as neuromuscular blocking agents,² and one report describes a case of sinus arrest in the presence of tubocurarine.³

Sinus arrest does not appear to have been described in association with median sternotomy during alcuronium-induced neuromuscular blockade, and should be borne in mind, especially in the patient who has received beta blockers.

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References

1. ATKINSON RS, RUSHMAN GB, LEE JA. *A synopsis of Anaesthesia*. 9th edn. London: Wright, 1982: 819.
2. HUNTER JM. Adverse effects of neuromuscular blocking drugs. *British Journal of Anaesthesia* 1987; **59**: 46-60.
3. NANDI PR, ASTLEY B. Bradycardia. *Anaesthesia* 1985; **40**: 1140.

Brain airway in anaesthesia for patients with juvenile chronic arthritis

The orthopaedic surgeons at this hospital operate almost weekly on patients with Juvenile Chronic Arthritis (Still's Disease). The problem of difficult airway management for anaesthesia in these children was solved in earlier years by the use of ketamine.¹ This created poor operating conditions and postoperative hallucinations despite the additional use of diazepam. Fibre-optically guided tracheal intubation and general anaesthesia is a possible alternative, but my personal success is not guaranteed particularly since we have insufficient funds to buy the appropriate fibroscope for the task.

Prototypes of Dr Brain's Laryngeal Mask Airway²⁻⁴ are

available for trial and I have found that mouth opening has permitted their use in most patients (15, so far). This unusual airway has proved a great success and has enabled me to secure the airway with few problems or delay and to use conventional inhalational techniques.

Prospective users should try the airway first on normal patients.

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B.L. SMITH

References

1. D'ARCY EJ, FELL RH, ANSELL BM, ARDEN GP. Ketamine and juvenile arthritis (Still's disease). *Anaesthesia* 1976; 31: 624-32.
2. BRAIN AIJ. The laryngeal mask—a new concept in airway

management. *British Journal of Anaesthesia* 1983; 55: 801-4.
3. BRAIN AIJ. Three cases of difficult intubation overcome by the laryngeal mask airway. *Anaesthesia* 1985; 40: 353-5.
4. Available from Colgate Medical, 1 Fairacres Estate, Dedworth Road, Windsor, Berks, SL4 4LE.

Bradycardia and facial surgery

We were interested to read the report by Drs Shearer and Wenstone of bradycardia during elevation of fractured zygomata (*Anaesthesia* 1987; 42: 1207-8) and by their interpretation of this as a variation of the oculocardiac reflex.¹

We have noticed bradycardia, sometimes associated with ventricular ectopic beats, when the maxilla is manipulated in patients who undergo a cosmetic maxillary osteotomy. A similar phenomenon was previously described and the bradycardia attributed to a variation of the oculocardiac reflex.¹ Since the parasympathetic supply of the face is carried in the trigeminal nerve, traction on areas within its distribution will result in parasympathetic stimulation and bradycardias in a manner analogous to traction on viscera. Perhaps it is time we discarded the term oculocardiac reflex in favour of trigeminocardiac reflex. It would then be clearer

that the oculocardiac reflex, although most commonly elicited, is just one manifestation of a more general reflex phenomenon. In addition, it would no longer be a surprise when traction on areas within the trigeminal distribution produced bradycardia.

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Reference

1. ROBIDEAUX V. Oculocardiac reflex caused by mid-face disimpaction. *Anesthesiology* 1978; 49: 433.

Analgesia during labour by continuous infusion epidurals

The provision of analgesia during labour by continuous infusion epidurals has many advantages over conventional top-ups, and is consequently becoming more popular. However, I am worried by some of the recommendations which are made to detect accidental intrathecal infusions.^{1,2} Confusion seems to have arisen in both these papers between what is a reasonable time interval in which to detect a high block from an *epidural* infusion and the time interval required to detect a true *subarachnoid* infusion. The recommendations are made more in hope¹ than on any hard facts relating to a safe² volume. Two hours is chosen by Li *et al.*² as a suitable frequency for testing at the T₅/T₆ level, while hourly tests at T₁₀ are suggested by Gaylard and Wilson.¹

It has been known for some time that in late pregnancy changes in posture may have profound effects on the levels of anaesthesia obtained with subarachnoid 0.5% plain bupivacaine.³ The level may be quite restricted, while patients remain on their side, but once placed supine on a wedge the level rises dramatically within a few minutes,

often accompanied by a precipitous decrease in blood pressure if proper precautions have not been taken.

To try and obtain some facts on the behaviour of subarachnoid infusions five patients had their spinal anaesthetics for elective Caesarean section induced in a novel manner. The women lay quietly on their right sides and an 18-gauge epidural needle was inserted at L_{2/3}. A 26-gauge spinal needle was guided through this into the subarachnoid space and 0.5% plain bupivacaine 3.0 ml was infused slowly into the spinal fluid over 30 minutes from a Vickers Treonic IP5 syringe pump set to deliver 6.0 ml/hour. A preload of at least 1000 ml Hartmann's solution was administered intravenously during the spinal infusion. A visual check was kept on the bupivacaine syringe to ensure that there were no gross errors in the volume delivered. The spinal needle was withdrawn after 30 minutes and an epidural catheter was inserted and quickly taped in place. Ephedrine (12 mg) was administered intravenously while the patients were positioned supine with a wedge under their right hip. The top part of Table 1 shows the analgesic levels obtained

Table 1. The spread of analgesia to pinprick in five pregnant patients near term.

Side	Patient number									
	1		2		3		4		5	
	L	R	L	R	L	R	L	R	L	R
<i>Time, minutes, patients on their sides</i>										
5	L ₃	0	L ₃	0	L ₃	0	L ₃	0	0	0
10	L ₃	0	L ₁	0	T ₁₁	L ₃	L ₂	0	0	0
15	L ₁	0	L ₁	0	T ₉	T ₁₀	T ₁₁	0	T ₁₀	0
20	L ₁	0	L ₁	0	T ₈	T ₈	T ₁₀	L ₃	T ₉	0
25	L ₁	0	T ₁₂	0	T ₈	T ₈	T ₁₀	L ₃	T ₉	0
30	T ₁₀	0	T ₁₂	0	T ₇	T ₆	T ₈	L ₃	T ₈	0
<i>Time, minutes, patients turned over onto wedge</i>										
2	T ₄	T ₆	T ₁₀	L ₁	T ₅	T ₅	T ₄	T ₄	T ₇	T ₁₀
5	T ₄	T ₅	T ₉	T ₁₀	T ₃	T ₃	T ₁	T ₁	T ₆	T ₇
10	T ₃	T ₃	T ₄	T ₄	T ₃	T ₃	C ₆	C ₆	T ₂	T ₂
15	T ₂	T ₂	T ₃	T ₃	T ₂	T ₂	T ₁	C ₈	T ₂	T ₂
30	T ₃	T ₃	T ₃	T ₃	T ₂	T ₂	T ₁	T ₁	T ₂	T ₂

during the first 30 minutes while the patients were quietly on their sides. The lower part of Table 1 shows what happens to these levels when the patient is repositioned with a wedge under the right hip.

Three points should be noted. Analgesia at 30 minutes is at or above the umbilicus in four of the five patients and is distinctly unilateral. There was a rapid rise in analgesic levels and both sides are now even within 5 minutes of turning over. All the patients required further increments of ephedrine to maintain their blood pressure within normal limits.

How this observed behaviour of a relatively small volume of 0.5% bupivacaine would compare with a larger volume of more dilute bupivacaine is unknown. Intuition suggests that the analgesic levels may be much higher with greater volumes, in both positions. These preliminary results indicate that considerable caution should be exercised in

the care of epidural infusions and suggest that blood pressure and analgesic levels should be monitored closely at not more than half-hourly intervals, and always for 5 to 10 minutes after a change in the patient's position.

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References

1. GAYLARD DG, WILSON IH, BALMER HGR. An epidural infusion technique for labour. *Anaesthesia* 1987; **42**: 1098-101.
2. LI DF, REES GAD, ROSEN M. Continuous extradural infusion of 0.0625% or 0.125% bupivacaine for pain relief in primigravid labour. *British Journal of Anaesthesia* 1985; **57**: 264-70.
3. RUSSELL IF. Posture and isobaric subarachnoid anaesthesia. The influence on spread of spinal anaesthesia with 'isobaric' 0.5% bupivacaine plain. *Anaesthesia* 1984; **39**: 865-7.

Sudden cardiac arrest during percutaneous nephrolithotomy

This is a report of an old problem¹ in a new guise.

The patient, a woman aged 32, had a staghorn calculus in the left kidney. Chest X ray and ECG were normal before operation; the haemoglobin was 13.6 g/100 ml, and the platelet count 199,000/ml. Serum sodium was 146 mmol/litre and potassium 4.7 mmol/litre.

Fentanyl 0.1 mg and atropine 0.5 mg were given 15 minutes before induction. General anaesthesia was induced with thiopentone 250 mg and suxamethonium 75 mg for tracheal intubation. Anaesthesia was continued with 66% N₂O and O₂ with controlled ventilation of the lungs, and muscle relaxation with pancuronium 6 mg. The patient was connected to an automatic ECG and blood pressure monitor for continual observation. The operative blood loss was small but one unit of blood was given. Fifteen to 18 litres of distilled water were used for irrigation of the kidney.

Bradycardia, 30-40 minute, occurred suddenly after 45 minutes. This was not reversible with atropine and developed rapidly into ventricular fibrillation and asystole. The plasma electrolytes were, sodium 135 mmol/litre, potassium 3.8 mmol/litre during the first hour, and after 1½ hours, the plasma sodium was 130 mmol/litre and the potassium 2.6 mmol/litre.

The patient developed cardiac arrest which, despite all the measures for resuscitation (external and internal cardiac

massage, defibrillation and cardiac stimulants), was not reversed. An autopsy showed a retroperitoneal haematoma (there was no evidence of pulmonary embolus or damage to any vessel). Nor was there any evidence during the operation of haemorrhage but in any case one unit of blood was given. The probable cause of death was electrolyte disturbance, particularly of potassium, because of absorption of large quantities of irrigation fluid (distilled water) which caused hypokalemia. The urologists now use sodium chloride 0.9% as an irrigation fluid.² The similarity between this event and irrigation of the prostatic bed is obvious.

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S. LOUCAS
J. KASTRIOTIS
C. DELIVELIOTIS
C. DIMOPOULOS

References

1. BENNET MJ, SMITH RW, FUCHS E. Sudden cardiac arrest during percutaneous ultrasonic nephrolithotomy. *Anesthesiology* 1984; **60**: 245-6.
2. SCHULTZ RE, HANNO PM, WEIN AJ, LEVIN RM, POLLACK HM, VAN ARSDALEN KN. Percutaneous ultrasonic lithotripsy: choice of irrigant. *Journal of Urology* 1983; **130**: 858-60.

Transport of a patient with an extremely low pulmonary compliance

We describe the successful transfer of a patient with extremely low pulmonary compliance to a hospital 72 miles away.

The patient was a 36-year-old woman who suffered from the adult respiratory distress syndrome after an episode of septic shock. Her lung function had deteriorated steadily for 9 weeks until it was considered that a heart-lung transplant offered the only hope of survival. Her lungs were ventilated by a Servo 900 C ventilator at the time of transfer with a minute volume of 29 litres/minute, a rate of 90 breaths/minute, an F_{IO_2} 0.7. The inspiratory fraction was set to 50% of each breath and the working pressure of the machine was 9.5 kPa. The inflation pressures ranged from 9-10 kPa. The mean tidal volume was 300 ml. She had a right pneumothorax which could not be fully re-expanded and there was a tracheostomy. Arterial blood gas analysis, on these settings showed P_{aCO_2} 8 kPa, and P_{aO_2} 10 kPa.

It was apparent that she needed to be ventilated continuously with the Servo 900 C during the period of transport

since she could not be adequately ventilated with the Oxylog ventilator or Mapleson C system which we normally use for patient transfer. We needed, in order to do this, to arrange a constant 240-volt power and gas supply for the Servo. The power was provided by an Uninterruptable Power Supply for transfer between Intensive Care Units and ambulance. We used a Static Inverter within the ambulance to convert the standard 12-volt output to a 240-volt output capable of supplying 150 watts. The Servo 900 C demand is 40 watts.

The Uninterruptable Power Supply is essentially a series of batteries which produce a power output at 240 volts. It is presented as a metal box measuring 60 cm × 30 cm × 30 cm and is easily transportable on a trolley. The power rating of our model was 500 VA which should be sufficient to deliver 40 watts for a period of 10 hours. It costs about £1000. Gases were provided from large air and oxygen cylinders with reducing valve adaptors to provide gases at 400 kPa. The connexions were of the quick release variety

so that cylinders could be changed in a matter of seconds. All power cables and gas hose pipes were of sufficient length so that the ventilator could be connected to the ambulance power and gas supply whilst it was outside the ambulance.

It was possible with these arrangements to deliver the patient in a smooth, unhurried manner. She was disconnected twice from the ventilator whilst the latter was lifted in and out of the ambulance, and she was ventilated with a Mapleson C system for approximately 45 seconds during these periods. The journey lasted 90 minutes and it took

20 minutes to transfer the patient between ICU and ambulance at each end.

We are very grateful to North East Essex Ambulance Control without whom it would not have been possible to move our patient.

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W.H. KONARZEWSKI
M. ROBINSON
D. THOMAS
D. ATREE

Grade III laryngoscopy—which is it?

A recent case report, by Eason *et al.* (*Anaesthesia* 1987; 42: 745–9) which described a patient with a C₂ vertebra fracture who required anaesthesia for emergency Caesarean section, included mention of a Grade III intubation—but was it?

Cormack & Lehane¹ defined Grade III laryngoscopy as one where only the epiglottis can be visualised and the illustration in their article clearly shows the whole of the epiglottis to be visible. One should remember that their classification, and conclusions drawn, were a theoretical exercise derived from the memories of colleagues' experiences and not based on any survey or hard facts. Samsoon & Young² more recently, however, refer to Grade III laryngoscopy as one where only the tip of the epiglottis can be seen. This certainly accords more with my experience and, interestingly, exactly fits the description of the case reported by Howells & Riethmuller.⁴

These definitions seem significantly different and there could be important implications. Firstly, in the accuracy of assessment and reliability of between-patient comparison false positives are likely. Despite the best possible head and neck position for the placement of the laryngoscope blade in the glosso-epiglottic fossa, this does not always enable the glottis to be seen if the epiglottis is large and overhanging. These could be construed as Grade III¹ but if the laryngoscope blade is placed posterior to the epiglottis this usually provides the solution. Trainees often do not appreciate that this can be done with the Macintosh blade. Similar situations can present when head movement or laryngoscopic manipulation are limited. This applies, for example, to patients with cervical fractures, on traction for fear of added injury to the spinal cord. Cricoid pressure may also cause confusion in grading.

Secondly, Grade III² seems an entity more similar to Grade IV and more difficult than Grade III.¹ However, the same techniques of intubation should be applicable, and useful, to Grade III² and Grade IV though a long Magill

laryngoscope blade or a modified/prism laryngoscope (e.g. the Belscope) could possibly help with the former only. On the other hand advice to attempt to intubate Grade III² but not Grade IV might not be valid. Either one ought to avoid both, or to attempt both.

Thirdly, the recommended simulated practice of Grade III¹ might not be entirely relevant to Grade III.² However, with the production of an appropriate curvature of the tube, successful insertion into the larynx of Grade III² and Grade IV should be possible. It is well recognised that smaller tube diameters and audible breath sounds aid location of the glottis. Correctly applied cricoid pressure ought to discourage oesophageal intubation. A potential advantage of methods such as blind nasal intubation, the lighted stylet and the fiberoptic laryngoscope, is that they depend on signs other than peroral laryngoscopic visualisation of the glottis to locate the larynx, that is, they circumvent or avoid the root cause of the problem.

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References

1. CORMACK RS, LEHANE J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; 39: 1105–11.
2. SAMSOON GLT, YOUNG JRB. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987; 42: 487–90.
3. HOWELLS TH, RIETHMULLER RJ. Signs of endotracheal intubation. *Anaesthesia* 1980; 35: 984–6.

A reply

We reported that only the tip of the epiglottis could be seen.

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J.R. EASON

Thermal injury associated with pulse oximetry

The use of pulse oximetry is increasingly common in both anaesthesia and intensive care. We wish to report a case of probable thermal injury to a patient's fingertips with this technique.

A 59-year-old woman had elective coronary artery bypass grafting, after which she required cardiovascular support including inotropes, intra-aortic balloon pumping and centrifugal left ventricular assist devices for 18, 12 and 5 days respectively. Skin perfusion was poor during this period. Postoperative monitoring included pulse oximetry with both Ohmeda Box 3700 and Datascope Accusat equipment using fingerprobes. It was often found difficult to obtain adequate signal quality, and probes were moved

between fingers in an attempt to achieve a good quality signal. The displayed oxygen saturations varied between 92% and 100%.

Twenty-one days after operation marks were noted on the index and ring fingers of the patient's left hand (Figs 1 and 2). The appearance of these marks was consistent with thermal, rather than pressure injury. Their location implicated the small thermal output from the light emitting diodes in the probe, which emit both in the red and infrared wavelengths (940 nm and 660 nm).

Ohmeda Ltd warn that, especially with their flexible probes in paediatric practice, thermal emission may warrant concern and probes should be checked every 2–4 hours.¹



Fig. 1

We feel that more emphasis should be placed on the possibility of thermal injury from pulse oximetry probes in the poorly perfused patient, and our present policy is to change probe sites hourly.

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D.H.T. SCOTT

Reference

1. Ohmeda Biox 3700 Manual, Ohmeda Ltd. 12/86.

A reply

The Accusat System contains a current limiter that prevents light emitting diodes in the probe from becoming over-



Fig. 2

driven, which removes the likelihood of an increase in temperature sufficient to cause a burn. Theories suggest poor peripheral perfusion and subsequent lack of blood cooling effect in an extremity, but we are not aware of any published evidence on this.

It is, however, generally recommended that all long-term probe sites are inspected regularly to ensure that no unnecessary pressure has been applied to the site, reducing tissue blood flow.

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C. ELDRED

Acute epiglottitis

The classical presentation of acute epiglottitis in children is well known. However, the following case is a reminder that whilst the diagnosis should always be considered in toxic children with airway problems, epiglottitis may also present in unusual ways.

A 14-month-old girl was recently admitted with a 3-hour history of acute irritability and excessive crying, after being given a chicken bone to chew by her father. Examination showed a fretful afebrile child who was drooling saliva but had no signs of airway obstruction and seemed systemically well. The lateral neck X ray was difficult to interpret due to rotation but appeared to show a foreign body fragment close to the hyoid and slight airway narrowing in the region of the epiglottis.

The child was not fasted but it was decided to expedite removal of the foreign body under general anaesthesia and she was taken immediately to theatre. An inhalational induction was performed during which mild inspiratory stridor developed. Laryngoscopy showed a swollen, erythematous and sloughing epiglottis. The posterior aspects of the arytenoids were visualised and nasotracheal intubation performed with a Portex 4.0 mm PVC tube. No foreign body could be found and a provisional diagnosis of acute epiglottitis was made. The child's trachea was left intubated and she was sedated on the ITU where a transient pyrexia developed, and was treated with humidified air and antibiotics. The size of nasal tube which allowed an air leak was smaller than expected and by 12 hours the leak itself had disappeared. *Haemophilus influenzae* type B bacilli were isolated from the throat but not the blood. Extubation

was performed 2 days later under general anaesthesia when there was no evidence of airway obstruction and the child was allowed home on day 5, treated with amoxycillin.

An unusual presentation of epiglottitis appears to have been precipitated early by the child eating chicken-bone fragments and subsequently being brought quickly to hospital by the worried parents. Appropriate treatment was promptly initiated once the correct diagnosis had been made, and the patient avoided the toxic and severe airway-compromising phase of the illness that is likely to have developed later. Reconsideration of the X ray, in the light of the new diagnosis, showed a normal hyoid bone, no foreign body and a swollen epiglottis. The original diagnosis of inhalation of a foreign body may have prejudiced the initial interpretation of the X ray.

Intubation was not particularly difficult under deep inhalational anaesthesia but with the risk of aspiration in an unfasted patient, the alternative technique such as a rapid sequence induction with thiopentone and suxamethonium might have been chosen: this could have led to a disastrous lack of airway control and inability to intubate.

It is vital, therefore, that in all children who present with any airway-related problem the possibility of the diagnosis of acute epiglottitis is considered, and where a compromised airway exists the use of an inhalational induction of anaesthesia is mandatory.

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P.R. HOWELL

Nitrous oxide and hearing loss

Dr Coe (*Anaesthesia* 1987; **42**: 1230-1) draws attention to one of the rarer problems associated with the use of nitrous oxide. But there are many other, more common, reasons for eschewing the use of nitrous oxide in modern anaesthesia.¹ One of these is that it makes possible the safe, simple and inexpensive use of totally closed system anaesthesia. I therefore cannot understand why Dr Coe writes about 'the trouble and expense of anaesthesia without nitrous oxide'. It is no trouble: it is not expensive and

it is very safe. It is the use of nitrous oxide which causes trouble, expense and unnecessary risks.

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Reference

1. BURNS THS. Closed circuit anaesthesia. *Anaesthesia* 1980; **35**: 1114-5.

Introducers for intubation

Gum elastic or neoplex bougies are frequently used to facilitate difficult tracheal intubation because they are relatively atraumatic to the tissues, but they seldom retain the shape to which they have been bent for long enough to permit successful intubation. A simple remedy is to hold the introducing end of the bougie under hot running water which immediately softens it, then bend it to the required

shape and turn on cold running water which fixes the bougie in the required shape, usually for long enough to permit intubation. If tracheal intubation fails, the technique may be repeated as required.

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J.S. PADDLE

An alternative to sedation during regional analgesia

Most anaesthetists are at least aware of, if not familiar with, the use of personal stereo cassette players for patients when regional analgesic techniques are employed. My own preference is the personal stereo radio headphones which are less cumbersome, more portable and convenient, less demanding on batteries and provide a comprehensive range of programme choice (music, chat shows and current affairs magazines). There is thus no need to build up an extensive and unwieldy library of cassettes to cater for all musical tastes among patients.

I have spent the last 6 months in a large orthopaedic centre where regional analgesic techniques for upper and lower limb surgery are widely practised: considerable numbers of middle aged and elderly patients have intrathecal, extradural, and brachial plexus blocks performed.

I ensured that the appropriate pre-anaesthetic 'work-up' was carried out when I visited patients pre-operatively. If a regional analgesic technique was decided upon, this was discussed at the visit before operation. Not surprisingly many patients expressed some apprehension about being awake during surgery but were reassured that 'something' would be given to help them relax and settle during the operation. These reassurances proved helpful in the alleviation of anxiety.

The appropriate regional analgesic technique was undertaken without an intravenous sedative or anxiolytic,

the prescribed oral premedicant being considered adequate, as is our normal practice. The patient was suitably positioned and prepared for the actual surgery after this. The stereo radio headphones were then offered with the station of choice (wavelength) selected and with the assurance that if the radio were not to the patient's satisfaction, the usual intravenous sedation would be given.

One patient in a group of 30 felt too nervous to continue to use the headphones, and requested sedation; the rest expressed pleasant surprise that they did not require peri-operative sedation, preferring, in retrospect, the use of headphones with the associated clarity of thought and lack of drowsiness both during and after operation. They also reported favourably on the degree of distraction and relaxation experienced during surgery and readily agreed that they would not hesitate to accept this method again.

Intravenous benzodiazepines are unpredictable in the elderly when used during regional analgesia and may cause complications. The acceptability of the above alternative has proved to be pleasing and interesting to me. Have others any experience with this technique and would they recommend it?

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R. ALLEN

Book reviews

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Principles and practice of regional anaesthesia 427
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- Anesthesia and uncommon pediatric diseases** 427
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Anaesthesia for cardiac surgery and allied procedures 428
 J.W.W. GOTHARD AND M.A. BRANTHWAITE

The ECG in anaesthesia and critical care

Edited by D.M. THYS AND J.A. KAPLAN. Pp. 267. Churchill Livingstone, 1987. £19.95.

In the introduction the editors state that this is the only book on electrocardiography specifically aimed at the anaesthetist. This is certainly not the case but that criticism apart, this is an admirable handbook.

It is aimed at the beginner so it includes some very clear chapters on the electrophysiology of the ECG and goes into some detail about optimum lead selection. The chapter sequence is a little disconcerting; the first two are concerned with the technology of the ECG; these are followed by four on clinical features of the abnormal ECG and then there are two further chapters on basic electrophysiology.

There is a useful chapter on the electrocardiographic effects of inhalational anaesthetic agents, which includes brief sections on intravenous drugs and relaxants. The effects of electrolyte disturbances are discussed very clearly. Other sections include the paediatric ECG and the ECG after cardiac surgery. The latter is particularly good on the recognition of the effects of surgical trauma on the myocardium. One of the most useful sections discusses the indications for the use of the different types of pacemakers and the anaesthetic considerations of pacemaker insertion and malfunction.

The book is well illustrated with diagrams and examples of ECGs which are well reproduced. Each chapter is accompanied by a reasonable selection of references although very few of these are of recent date and even fewer originate from outside the USA.

Overall I found it a very pleasant book to read and one which it is possible to dip into because of the chapter headings and the quality of the index. If I have a criticism it is that the therapeutic implications of abnormalities in the ECG are dealt with very selectively and have to be sought specifically.

J.C. STODDART

Principles and practice of regional anaesthesia

Edited by J.A.W. WILDSMITH AND E.N. ARMITAGE. Pp. 200. Churchill Livingstone, 1987. £35.00.

There is no doubt that regional anaesthesia is increasing in popularity and that there is more to the method than depositing sufficient local anaesthetic drug around the appropriate nerves to numb the offending part. Knowledge of the pharmacokinetic and pharmacodynamic effects of the drugs has increased considerably in the last few years, allowing a more rational choice of drug for any particular patient. Care of the patient in receipt of a regional block and the prevention and management of potential complications have also been emphasised. Any book on regional anaesthesia must cover these general aspects as well as describing the anatomy and techniques of the blocks.

At last there is a British text along these lines and what a lovely book it is. No longer do we have to go foreign to find out how to perform a block; it is all here under one cover. The opening chapters concern history, features of regional anaesthesia, pain pathways and pharmacology. These are followed by an excellent dissertation on the management of regional anaesthesia by Charlton; essential reading. The remainder of the book is devoted to the relevant anatomy and techniques of the various regional anaesthetic procedures, including complications. The clarity of description of these is undoubtedly due to the fact that the authors all practise these techniques, and do not just write about them. The coloured illustrations are superb.

This book is recommended to all anaesthetists wishing to learn or improve their regional anaesthetic techniques and no doubt it will become a standard for all those taking the Part III Fellowship examination. I was very pleased to have been asked to review it, otherwise I would have been forced to buy it.

M. MORGAN

Anesthesia and uncommon pediatric diseases

Edited by J. KATZ AND D.J. STEWARD. Pp. 549. W.B. Saunders, 1987. £59.00.

This excellent book results from the combined efforts of the two editors, one from San Diego and well known for a similar title in adult anaesthesia and the other from Vancouver, who is a highly respected paediatric anaesthetist, together with 21 co-authors. The resulting production is of an extremely high standard, all the contributors are anaesthetists and originate from Canada, USA, or England, and the text reflects their dedication and commitment to anaesthesia in children. The 18 chapters deal with disorders of the six body systems, together with specialised subjects such as infectious diseases, paediatric head and neck syndromes, ophthalmic and otolaryngological, genetic metabolism, orthopaedic, skin and connective tissue, immune and allergic, blood, and neuromuscular diseases. The first two chapters serve as an introduction to paediatric anaesthesia and are devoted to anatomy, physiology and pharmacology. The editors have done well to avoid too much overlap of topics.

Potential purchasers should not assume that the contents are entirely devoted to esoteric diseases and conditions encountered in paediatric anaesthesia. Conditions that many paediatric anaesthetists regard as normally presenting for routine operation, such as well known neonatal conditions, cleft palate, orchidopexy and congenital pyloric stenosis are all covered in the appropriate chapters. However, it is in the detailed description of rare abnormalities and their implications for the anaesthetist that this book excels. Thus the syndromes associated with congenital craniofacial deformities for example, are well classified and described, and the anaesthetic requirements delineated. The index allows a rapid referral to the appropriate chap-

ters, which can then be cross indexed with other chapters where the syndrome affects a number of body systems e.g. Goldenhar syndrome. The majority of the chapters not only contain a most impressive bibliography (the chapter on diseases of the renal system contains 702 references) but also an important list of references for further reading.

This book is undoubtedly the definitive reference work for the full-time and the occasional paediatric anaesthetist, confronted with the prospect of providing anaesthesia for an infant with an unusual paediatric condition or disease. The reviewer has been delighted to comment on this book; the production is excellent, and the text reads well and easily. It should be regarded as an essential companion to standard textbooks on paediatric anaesthesia and readily available in all anaesthetic departments which deal with specialised children's operations. The price, considering the wealth of information the volume contains, is certainly not excessive. The editors and authors are to be congratulated on an outstanding contribution to the literature of paediatric anaesthesia.

G.H. BUSH

Anaesthesia for cardiac surgery and allied procedures

J.W.W. GOTHARD, with contributions from M.A. BRANTHWAITE. Pp. ix + 285. Blackwell Scientific Publications, 1987. £29.50.

The rapidly changing techniques in cardiac surgery continue to be reflected by the authors, in the third edition of this notable and popular textbook to be published in just over a decade.

The book takes the reader through the subject of cardiac anaesthesia in a logical and coherent manner. The first two chapters which deal with pertinent applied physiology and pathophysiology of cardiac disease, are complemented by a short chapter which covers the subject of cardiac diagnostic procedures. This logical approach is continued, in broad terms, with chapters on pre-operative assessment of the

patient followed by preparation and management of patients during anaesthesia and cardiopulmonary bypass. Every cardiac surgical unit in the UK is aware that there is an increasing emphasis on the management of ischaemic heart disease and this is reflected in the text. However, sections on the anaesthetic significance of specific conditions, which include chronic valvular heart disease and closed cardiac procedures, complement the descriptive technique. The authors' philosophy of providing a text for the trainee rather than for the specialist is supported by a commendable didactic approach to the anaesthesia and postoperative management of patients.

The final relatively extensive chapter on congenital heart disease and the principles of paediatric cardiac surgery again follows the same didactic but sensible approach to the subject, with sections on diagnosis and principles of anaesthesia for open and closed cardiac surgery, and anaesthetic implications of specific cardiac lesions in children.

The format of the text is unchanged from previous editions and includes a list of contents at the beginning, and references at the end of each chapter. The list of over 300 references with many as recent as 1986, are not acknowledged in the text, but arranged under subject headings and intended as 'further reading'. The text is further complemented with the liberal interspersed of 61 figures (including chest radiographs) and 30 tables.

The authors' aspiration to provide an extensively revised, up-to-date text for trainee anaesthetists, with relevant sections on cardiac conditions common in the third world, is fulfilled in this commendable book.

D.T. PEARSON

Book received

We thank the publisher for the following book, which we may review in a future issue.

Cardiopulmonary cerebral resuscitation

P. SAFAR AND N.G. BIRCHER. Pp. xvii + 464. W.B. Saunders, 1987. £11.50.

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for January 1988. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Pharmacology

Adrenergic drugs and their antagonists

- Comparative pharmacokinetics of intravenous propranolol in obese and normal volunteers. CHEYMOL G, POIRIER JM *et al. Journal of Clinical Pharmacology* 1987; **27**: 874.
- The effects of naloxone and timolol on plasma catecholamine levels during short-term dynamic exercise. GULLESTAD L, DOLVA LO *et al. Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47**: 847.
- The comparative effects of ICI 118551 and propranolol on essential tremor. JEFFERSON D, WHARRAD HJ *et al. British Journal of Clinical Pharmacology* 1987; **24**: 729.

Anaesthetic agents

- Toxicological interactions between carbon monoxide and carbon dioxide. LEVIN BC, PAABO M *et al. Toxicology* 1987; **47**: 135.
- Hepatotoxicity and death following two enflurane anaesthetics. PAULL JD, FORTUNE DW. *Anaesthesia* 1987; **42**: 1191.
- Generation of halothane-induced immune response in a guinea pig model of halothane hepatitis. SIADAT-PAJOUH M, HUBBARD AK *et al. Anesthesia and Analgesia* 1987; **66**: 1209.
- Effects of halothane and other chlorinated hydrocarbons on alpha-2-adrenoreceptors in the mouse cortex. WIKBERG JES, HEDE AR, POST C. *Pharmacology and Toxicology* 1987; **61**: 271.

Analgesic agents

- Oral administration of codeine in the presence of ethanol: a pharmacokinetic study in man. BODD E, BEYLICH KM *et al. Pharmacology and Toxicology* 1987; **61**: 297.
- Serum morphine concentrations after buccal and intramuscular morphine administration. FISHER AP, FUNG C, HANNA M. *British Journal of Clinical Pharmacology* 1987; **24**: 685.
- Binding of naloxone to human T lymphocytes. MADDEN JJ, DONAHOE RM *et al. Biochemical Pharmacology* 1987; **36**: 4103.
- Meptazinol and pentazocine: plasma catecholamines and other effects in healthy volunteers. MANNER T, KANTO J *et al. British Journal of Clinical Pharmacology* 1987; **24**: 689.
- Blockade of the development of analgesic tolerance to morphine by concurrent treatment with opioid—but not non-opioid-mediated stress in mice. TAKAHASHI M, DEGUCHI Y, KANETO H. *Japanese Journal of Pharmacology* 1988; **46**: 1.

Muscle relaxants

- Interactions between gallamine and muscarinic receptors: allosterism and subpopulation specificity are separate phenomena. ELLIS J, SEIDENBERG M. *European Journal of Pharmacology* 1987; **144**: 39.
- Muscle pathology in the neuroleptic malignant syndrome. MARTIN DT, SWASH M. *Journal of Neurology* 1987; **235**: 120.
- Antimuscarinic action of methoctramine, a new cardioselective M-2 muscarinic receptor antagonist, alone and in combination with atropine and gallamine. MELCHIORRE C, ANGELI P *et al. European Journal of Pharmacology* 1987; **144**: 117.

Other drugs

- Drug metabolism in the elderly. LOI CM, VESTAL RE. *Pharmacology and Therapeutics* 1988; **36**: 131.
- Plasma protein binding of clonazepam in hepatic and renal insufficiency and after hemodialysis. PACIFICI GM, VIANI A *et al. Therapeutic Drug Monitoring* 1987; **9**: 369.
- New synthetic antagonists of bradykinin. SCHACHTER M, UCHIDA Y *et al. British Journal of Pharmacology* 1987; **92**: 851.
- Plasma haloperidol and clinical response: a role for reduced haloperidol in antipsychotic activity? SHOSTAK M, PEREL JM *et al. Journal of Clinical Psychopharmacology* 1987; **7**: 394.
- Classification of cephalosporins. WILLIAMS JD. *Drugs* 1987; **34** (Suppl. 2): 15.
- Abuse liability of benzodiazepines. WOODS JH, KATZ JL, WINGER G. *Pharmacological Reviews* 1987; **39**: 254.

Apparatus

- Determination of cardiac output with a modified Fick method using estimated instead of measured oxygen consumption. DALE J, JESPERSEN L. *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47**: 759.
- Effect of new vacutainer blood collection tubes on plasma lidocaine concentrations. LOPEZ LM, SEN A *et al. Therapeutic Drug Monitoring* 1987; **9**: 439.

Complications

- Accounting for perioperative deaths. LEADING ARTICLE. *Lancet* 1987; **2**: 1369.
- Lessons from the confidential enquiry into perioperative deaths in three NHS regions. LUNN JN, DEVLIN HB. *Lancet* 1987; **2**: 1384.

General anaesthetic procedures

- Oral premedication with clonidine—effects on stress responses during general anaesthesia. POUTTU J, SCHEININ B *et al. Acta Anaesthesiologica Scandinavica* 1987; **31**: 730.

General interest

- An anesthesiologists philosophy on medical clearance for surgical patients. CHOI JJ. *Archives of Internal Medicine* 1987; **147**: 2090.
- What is the cause of the carcinoid flush? GRAHAMSMITH DG. *Gut* 1987; **28**: 1413.
- Idiopathic pulmonary fibrosis: a historical review. HOMOLKA J. *Canadian Medical Association Journal* 1987; **137**: 1003.
- The arachidonic acid cascade: an immunologically based review. JANNIGER CK, RACIS SP. *Journal of Medicine* 1987; **18**: 69.
- Central nervous system dysfunction in acquired immunodeficiency syndrome. LEVY RM, BREDESEN DE. In: ROSEMBLUM ML *et al. eds. Aids and the nervous system*. New York: Raven Press, 1988; 29.
- Prions and neurodegenerative diseases. PRUSINER SB. *New England Journal of Medicine* 1987; **317**: 1571.
- Ocular myopathies. A nosological study of 49 cases. SERRATRICE G, PELLISSIER JF. *La Presse Medicale* 1987; **16**: 1969.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request, and at a modest charge, a new additional service to our readers. References from January 1984 have been entered on data base. The data are held on Dbase II, cpm 86 and on Dbase III, MsDos and are available on disc, together with a program providing search facilities. Enquiries direct to Dr Kaufman at the above address please.

Spinal and epidural analgesia

Decrease in serum potassium concentration during epidural anaesthesia. HAHN RG. *Acta Anaesthesiologica Scandinavica* 1987; 31: 680.

Spinal opioids

- Cardiovascular effects of enkephalins. FEUERSTEIN G, SIREN AL. *ISI Atlas of Science—Pharmacology* 1987; 1: 280.
- Opioid analgesia at peripheral sites: a target for opioids released during stress and inflammation? JORIS JL, DUBNER R, HARGREAVES KH. *Anesthesia and Analgesia* 1987; 66: 1277.
- Effect of chronic treatment with tricyclic antidepressants upon antinociception induced by intrathecal injection of morphine and monoamines. KELLSTEIN DF, MALSEED RT *et al.* *Neuropharmacology* 1988; 27: 1.
- Role of endogenous opioids on ventilation and chemical control of breathing in pentobarbitone-anesthetized rats. MAUSER PJ, CHAPMAN RW. *Pharmacology* 1987; 35: 317.
- Age predicts effective epidural morphine dose after abdominal hysterectomy. READY LB, CHADWICK HS, ROSS B. *Anesthesia and Analgesia* 1987; 66: 1215.
- Involvement of adenosine in the spinal antinociceptive effects of morphine and noradrenaline. SWEENEY MI, WHITE TD, SAWYER J. *Journal of Pharmacology and Experimental Therapeutics* 1987; 243: 657.
- Distribution of opioid binding sites in spinal cord. TRAYNOR JR, WOOD MS. *Neuropeptides* 1987; 10: 313.

Obstetric anaesthesia and analgesia

- Pharmaceutical agents in pregnancy. KNORR K. *Archives of Gynecology and Obstetrics* 1987; 241 (Suppl.): S46.
- Disposition of the adrenergic blocker metoprolol and its metabolite OH-metoprolol in maternal plasma, amniotic fluid and capillary blood of the neonate. LINDBERG S, LUNDEBERG P *et al.* *European Journal of Clinical Pharmacology* 1987; 33: 363.
- Fetal breathing movements are not a reliable predictor of continued lung development in pregnancies complicated by oligohydramnios. MOESSINGER AC, FOX HE *et al.* *Lancet* 1987; 2: 1297.
- An oxytocin inhibitor for suppressing preterm labour. TURNBULL AC. *British Journal of Obstetrics and Gynaecology* 1987; 94: 1009.

Paediatric anaesthesia and intensive care

- Percutaneous respiration in the newborn infant. Effect of gestation and altered ambient oxygen concentration. CARLIDGE PHT, RUTTER N. *Biology of the Neonate* 1987; 52: 301.
- Alveolar hypoxia increases small pulmonary wedge pressure in awake young lambs. HAZINSKI TA, KENNEDY KA. *Pediatric Research* 1987; 22: 675.
- Effects of birth-related events on blood flow distribution. IWAMOTO HS, TEITEL D, RUDOLPH AM. *Pediatric Research* 1987; 22: 634.
- Augmentation of cardiac output with intravenous catecholamines in unanesthetized hypoxemic newborn lambs. O'LAUGHLIN MP, FISHER DJ *et al.* *Pediatric Research* 1987; 22: 667.
- Effect of increased intracranial pressure on blood pressure, heart rate, respiration and catecholamine levels in neonatal and adult rabbits. OGILVY CS, DUBOIS AJB. *Biology of the Neonate* 1987; 52: 327.
- Fetal heart rate monitoring during labour—too frequent intervention, too little benefit. PRENTICE A, LIND T. *Lancet* 1987; 2: 1375.
- Respiratory water loss in relation to activity in full term infants on their first day after birth. RIESENFELD T, HAMMARLUND K, SEDIN G. *Acta Paediatrica Scandinavica* 1987; 76: 889.
- Altered cardiac repolarization in some victims of sudden infant death syndrome. SADEH D, SHANNON DC *et al.* *New England Journal of Medicine* 1987; 317: 1501.
- Chronic respiratory failure in infants with prolonged ventilator dependency. SCHREINER MS, DOWNES JJ *et al.* *Journal of the American Medical Association* 1987; 258: 3398.
- Early intravenous indomethacin prolongs respiratory support in very low birth weight infants. VINCE M, ALLEN A *et al.* *Acta Paediatrica Scandinavica* 1987; 76: 894.

Cardiovascular system

Physiology

- Bedside evaluation of sinus bradycardia: usefulness of atropine test in discriminating organic from autonomic involvement of sinus automaticity. CAPPATO R, ALBONI P *et al.* *American Heart Journal* 1987; 114: 1384.
- Role of von Willebrand factor in the vessel wall. DE GROOT PG, SIXMA JJ. *Seminars in Thrombosis and Hemostasis* 1987; 13: 416.
- Catecholamine metabolism during pacing-induced angina pectoris and the effect of transcutaneous electrical nerve stimulation. EMANUELSSON H, MANNHEIMER C *et al.* *American Heart Journal* 1987; 114: 1360.
- Cardiovascular responses to upright tilting in healthy subjects. HAINSWORTH R, AL-SHAMMA YMH. *Clinical Science* 1988; 74: 17.
- Regional coronary blood flow in canine hemorrhagic shock. HORTON JW, POEHLMANN DS. *Circulatory Shock* 1987; 23: 271.
- Thrombin-induced intravascular coagulation: role in vascular injury. KAPLAN JE, MALIK AB. *Seminars in Thrombosis and Hemostasis* 1987; 13: 398.
- Skeletal muscle blood flow capacity: role of muscle pump in exercise hyperemia. LAUGHLIN MH. *American Journal of Physiology* 1987; 253 (Part 2): H993.
- Fibrinogen, fibrinogen receptors, and the peptides that inhibit these interactions. PLOW EF, MARGUERIE G, GINSBERG M. *Biochemical Pharmacology* 1987; 36: 4035.
- Differences in mortality from acute myocardial infarction between coronary care unit and medical ward: treatment or bias? REZNIK R, RING I *et al.* *British Medical Journal* 1987; 295: 1437.
- Hypokalemia after cardioversion from ventricular tachycardia induced in the electrophysiology laboratory. SALERNO DM, DUNBAR D *et al.* *American Heart Journal* 1987; 114: 1389.
- Prediction of complex atrioventricular conduction rhythms in humans with use of the atrioventricular nodal recovery curve. SHRIER A, DUBARSKY H *et al.* *Circulation* 1987; 76: 1196.
- Measurements of base blood pressure during sleep and its clinical significance in hypertensive patients. TOCHIKUBO O, OCHIAI H *et al.* *Japanese Circulation Journal* 1987; 51: 1174.

Treatment and medication

- Effects of indomethacin on pulmonary hemodynamics and gas exchange in patients with pulmonary artery hypertension, interference with hydralazine. ADNOT S, DEPOUILLOY C *et al.* *American Journal of Respiratory Disease* 1987; 136: 1343.
- Mortality in heart failure: clinical variables of prognostic value. CLELAND JGF, DARGIE HF, FORD I. *British Heart Journal* 1987; 58: 572.
- Survival from cardiac arrest in the accident and emergency department. COPE AR, QUINTON DN *et al.* *Journal of The Royal Society of Medicine* 1987; 80: 746.
- Hemostasis after open-heart surgery with extreme or moderate hemodilution. DALE J, LILLEAASEN P, ERIKSSON J. *European Surgical Research* 1987; 19: 339.
- Predictors of sudden death up to 18 years after a first attack of unstable angina or myocardial infarction. DALY LE, HICKEY N *et al.* *British Heart Journal* 1987; 58: 567.
- High-risk aortic aneurysm repair with partial cardiopulmonary bypass. FIORE WM, OURIEOL K *et al.* *Journal of Vascular Surgery* 1987; 6: 563.
- Oral verapamil and calcium infusion in patients with sick sinus syndrome. MIDTBO K. *Pharmacology and Toxicology* 1987; 61: 293.
- Antihypertensive effect of enalapril in essential hypertension—role of prostacyclin. OPARIL S, HORTON R *et al.* *American Journal of the Medical Sciences* 1987 294: 395.
- Effect of aprotinin on need for blood transfusion after repeat open-heart surgery. ROYSTON D, BIDSTRUP BP *et al.* *Lancet* 2: 1289.
- Preoperative predictors of mortality risk in ruptured abdominal aortic aneurysm. SHACKLETON CR, SCHECHTER MT *et al.* *Journal of Vascular Surgery* 1987; 6: 583.
- Effect of esmolol on the ventricular fibrillation threshold. WALLS DE, WEDEL VA *et al.* *Pharmacology* 1988; 36: 9.

Respiration

Physiology

- Cardiovascular and respiratory effects of adenosine in conscious man: evidence for chemoreceptor activation. BIAGGIONI I, OLAFSSON B *et al. Circulation Research* 1987; **61**: 779.
- Arteriolar oxygen reactivity: where is the sensor? JACKSON WF. *American Journal of Physiology* 1987; **253** (Part 2): H1120.
- Alveolar carbon monoxide: a comparison of methods of measurement and a study of the effect of change in body posture. KIRKHAM AJT, GUYATT AR, CUMMING G. *Clinical Science* 1988; **74**: 23.
- High frequency chest wall oscillation in patients with chronic air-flow obstruction. PIQUET J, BROCHARD L *et al. American Journal of Respiratory Disease* 1987; **136**: 1355.
- Expiratory muscles and exercise limit in patients with chronic obstructive pulmonary disease. VERGERET J, KAYS C *et al. Respiration* 1987; **52**: 181.
- Dynamics of pulmonary gas exchange. WHIPP BJ. *Circulation* 1987; **76** (Suppl.): 18.

Treatment and medication

- High-dose corticosteroids in patients with the adult respiratory distress syndrome. BERNARD GR, LUCE JM *et al. New England Journal of Medicine* 1987; **317**: 1565.
- Intermittent negative pressure ventilation in the treatment of respiratory failure in progressive neuromuscular disease. BRAUN SR, SUFT RL *et al. Neurology* 1987; **37**: 1874.
- A program for transtracheal oxygen delivery: assessment of safety and efficacy. CHRISTOPHER KL, SPOFFORD BT *et al. Annals of Internal Medicine* 1987; **107**: 802.
- Protective effect of a-human atrial natriuretic polypeptide (a-hANP) on chemical-induced pulmonary edema. IMAMURA T, OHNUMA N *et al. Life Sciences* 1988; **42**: 403.
- Metabolic and respiratory changes during weaning from mechanical ventilation. KEMPER M, WEISSMAN C *et al. Chest* 1987; **92**: 979.
- Treatment of lower respiratory infections. MACFARLANE JT. *Lancet* 1987; **2**: 1446.
- Phrenic nerve stimulation in normal subjects and in patients with diaphragmatic weakness. MIER A, BROPHY C *et al. Thorax* 1987; **42**: 885.
- Effects of continuous positive airway pressure in acute asthma. SHIVARUM U, DONATH J *et al. Respiration* 1987; **52**: 157.

Central nervous system

Physiology

- Cerebral blood flow autoregulation during intracranial hypertension in hypoxic lambs. BOREL CO, BACKOFEN JE *et al. American Journal of Physiology* 1987; **253** (Part 2): H1342.
- Sleep-related breathing impairment in myotonic dystrophy. CIRIGNOTTA F, MONDINI S *et al. Journal of Neurology* 1987; **235**: 80.
- Sleep onset REM periods observed after sleep interruption in normal short and normal long sleeping subjects. FUKUDA K, MIYASITA A, INUGAMI M. *Electroencephalography and Clinical Neurophysiology* 1987; **67**: 508.
- Human brain dopamine receptors in children and aging adults. SEEMAN P, BZOWEJ NH *et al. Synapse* 1987; **1**: 399.

Treatment and medication

- Antiepileptic drugs and the electroencephalogram. DUNCAN JS. *Epilepsia* 1987; **28**: 259.
- Current medical and surgical therapy for cerebrovascular disease. GROTTA JC. *New England Journal of Medicine* 1987; **317**: 1505.

Endocrine and metabolic

Physiology

- Cardiovascular responses to stress: the role of opioid peptides. BOULOUX PMG. *Bailliere's Clinical Endocrinology and Metabolism* 1987; **1**: 439.
- Degradation and transport of AVP by proximal tubule. CARONE FA, CHRISTENSEN EI, FLOURET G. *American Journal of Physiology* 1987; **253** (Part 2): F1120.

- Nicotinic and M1-muscarinic, M2-muscarinic cholinergic control of ACTH response to insulin-induced hypoglycaemia in man. COIRO V, PASSERI M *et al. Acta Endocrinologica* 1987; **116**: 531.
- Insensible water loss and its assessment in adult patients—a review. COX P. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 771.
- Arginine vasopressin (AVP) and corticotropin releasing factor (CRF)-41 content of the anterior pituitary does not correlate with presumed secretion rates. DOHANICS J, LINTON EA *et al. Neuroendocrinology—Letters* 1987; **9**: 373.
- Stress and the pituitary-adrenal axis. GAILLARD RC, AL-DAMLUJI S. *Bailliere's Clinical Endocrinology and Metabolism* 1987; **1**: 319.
- Opiates, opioid peptides and the release of vasopressin. GREIDANUS TBV. In: RUNBERG A *et al. eds. Comparative Pathophysiology of Regulatory Peptides*. Basel: S. Karger, 1988: 112.
- Bradykinin in carcinoid syndrome. GUSTAFSEN J, BOESBY S *et al. Gut* 1987; **28**: 1417.
- Lesions of A1 noradrenergic cells affect AVP release and heart rate during hemorrhage. HEAD GA, QUAIL AW, WOODS RL. *American Journal of Physiology* 1987; **253** (Part 2): H1012.
- Enhanced hepatic insulin sensitivity, but peripheral insulin resistance in patients with type-1 (insulin-dependent) diabetes. HOTHER-NIELSEN O, SCHMITZ O *et al. Diabetologia* 1987; **30**: 834.
- Minireview: Calcium release in smooth muscle. KARAKI H, WEISS GB. *Life Science* 1988; **42**: 111.
- Physiology and pathophysiology of the hypothalamo-pituitary-adrenal axis. LOWRY PJ, LINTON EA, JACKSON S. In: RUNBERG A *et al. eds. Comparative pathophysiology of regulatory peptides*. Basel: S. Karger 1988: 1.
- Meptazinol and pentazocine: effects on prolactin, growth hormone and vasopressin levels in plasma. MANNER T, KANTO J *et al. Pharmacology and Toxicology* 1987; **61**: 301.
- Opioid peptides in blood and cerebrospinal fluid during acute stress. OWENS PC, SMITH R. *Bailliere's Clinical Endocrinology and Metabolism* 1987; **1**: 415.
- Splanchnic and renal hemodynamic responses to intraportal infusion of glucagon. PREMEN AJ. *American Journal of Physiology* 1987; **253** (Part 2): F1105.
- Corticosteroid effects on morphine-induced antinociception as a function of two types of corticosteroid receptors in brain. RATKA A, VELDHUIS HD, DE KLOET ER. *Neuropharmacology* 1988; **27**: 15.
- Hormone receptor interactions: an overview. ROTH J, LESNIAK M, HILL JM. *Kidney International* 1987; **32** (Suppl.): S56.
- Sympatho-adrenal and pituitary hormone responses during and immediately after thoracic surgery—modulation by 4 different pain treatments. SCHEININ B, SCHEININ M *et al. Acta Anaesthesiologica Scandinavica* 1987; **31**: 762.
- Central and systemic arginine vasopressin release and effects of anesthesia and surgery in dogs. SIMONOPPERMANN C, GRAY DA *et al. In: RUNBERG A et al. eds. Comparative pathophysiology of regulatory peptides*. Basel: S. Karger, 1988: 126.
- Catecholamine-glucocorticoid interactions during surgical stress. UDELSMAN R, GOLDSTEIN DS *et al. Journal of Surgical Research* 1987; **43**: 539.

Endocrine and metabolic

Treatment and medication

- Prolonged insulin resistance following insulin-induced hypoglycaemia. CLORE JN, BRENNAN JR *et al. Diabetologia* 1987; **30**: 851.
- A guide to the clinical use of the somatostatin analogue SMS 201-995 (Sandostatin). LAMBERTS SWJ. *Acta Endocrinologica* 1987; **116** (Suppl. 286): 54.

Pain

Physiology

- Plasma beta-endorphin during clinical and experimental ischaemic pain. BACH FW, FAHRENKRUG J *et al. Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47**: 751.

Treatment and medication

- Use of patient-controlled analgesia for management of acute pain. WHITE PF. *Journal of the American Medical Association* 1988; **259**: 243.

Other

Physiology

Lower esophageal sphincter pressure and gastroesophageal pressure gradients in excessively obese patients. MERCER CD, WREN SF. *Journal of Medicine* 1987; **18**: 135.

Treatment and medication

Preclinical overview of nabumetone: pharmacology, bioavailability, metabolism, and toxicology. MANGAN FR, FLACK JD, JACKSON D. *American Journal of Medicine* 1987; **83**: 6.

Erratum

Anaesthesia, 1988, Volume 43, pages 104–106

Peri-operative dreaming in paediatric patients who receive suxamethonium

E. P. O'SULLIVAN, D. CHILDS AND G. H. BUSH

In the second line of the Summary on p.104 the dosage of tubocurarine was given incorrectly as 80 mg/kg. The correct version should read:

A prospective study is described of peri-operative dreaming in 144 paediatric patients aged 5–14 years who received suxamethonium for day case surgery. No case of awareness was elicited. One group received pretreatment with 80 µg/kg tubocurarine. The incidence of dreaming in the 72 patients who were not pretreated was 16.7% compared with 2.8% in the patients pretreated with tubocurarine.

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Examples of correct form of references
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JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294**: 687–90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN. Pathogenic properties of invading micro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457–72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968–June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10: Data from the National Health Survey, No. 69*) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

TABLES

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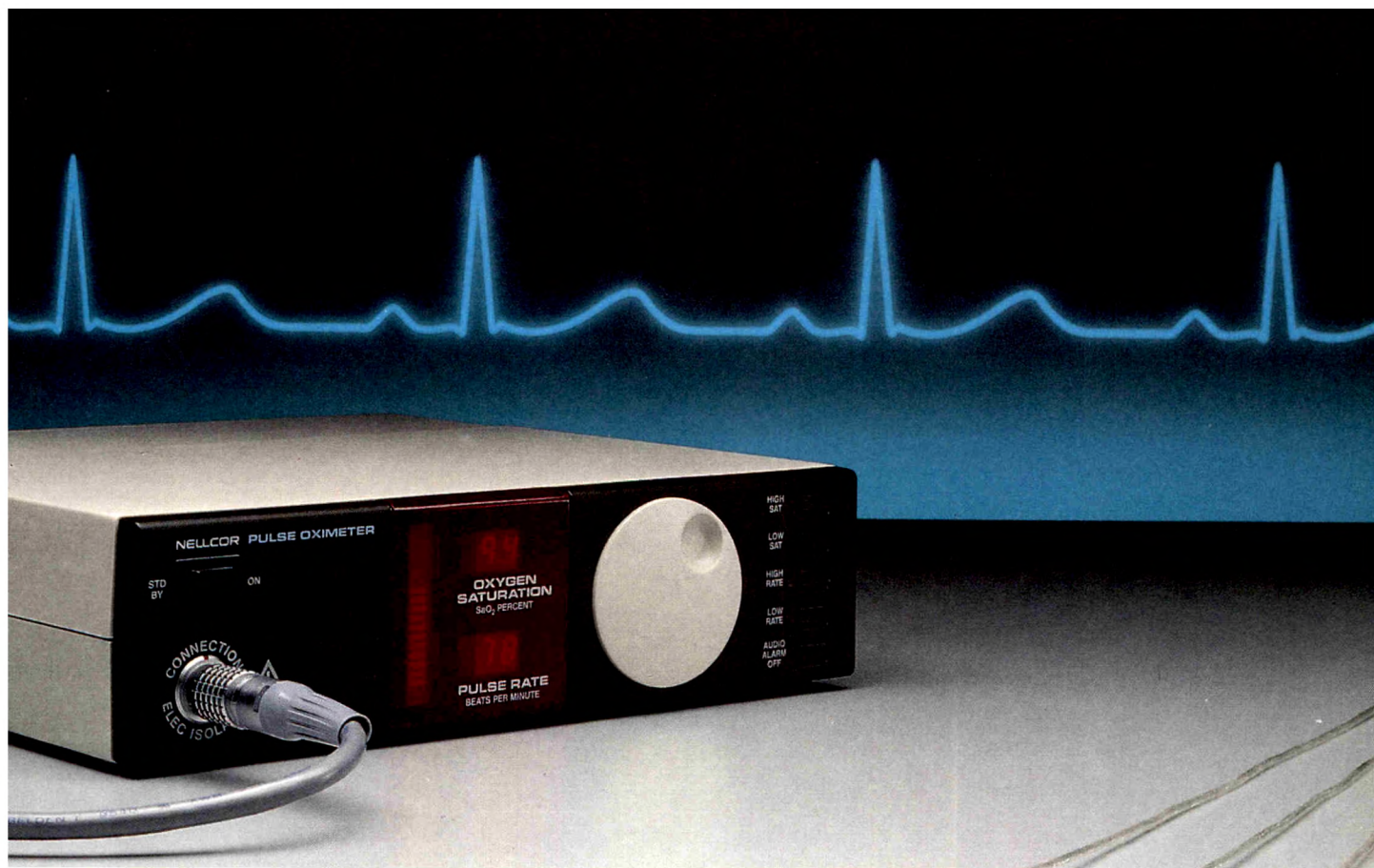
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Journal of the Association of Anaesthetists of Great Britain and Ireland

Volume 43 Number 6 June 1988



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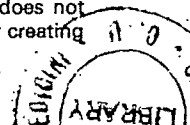
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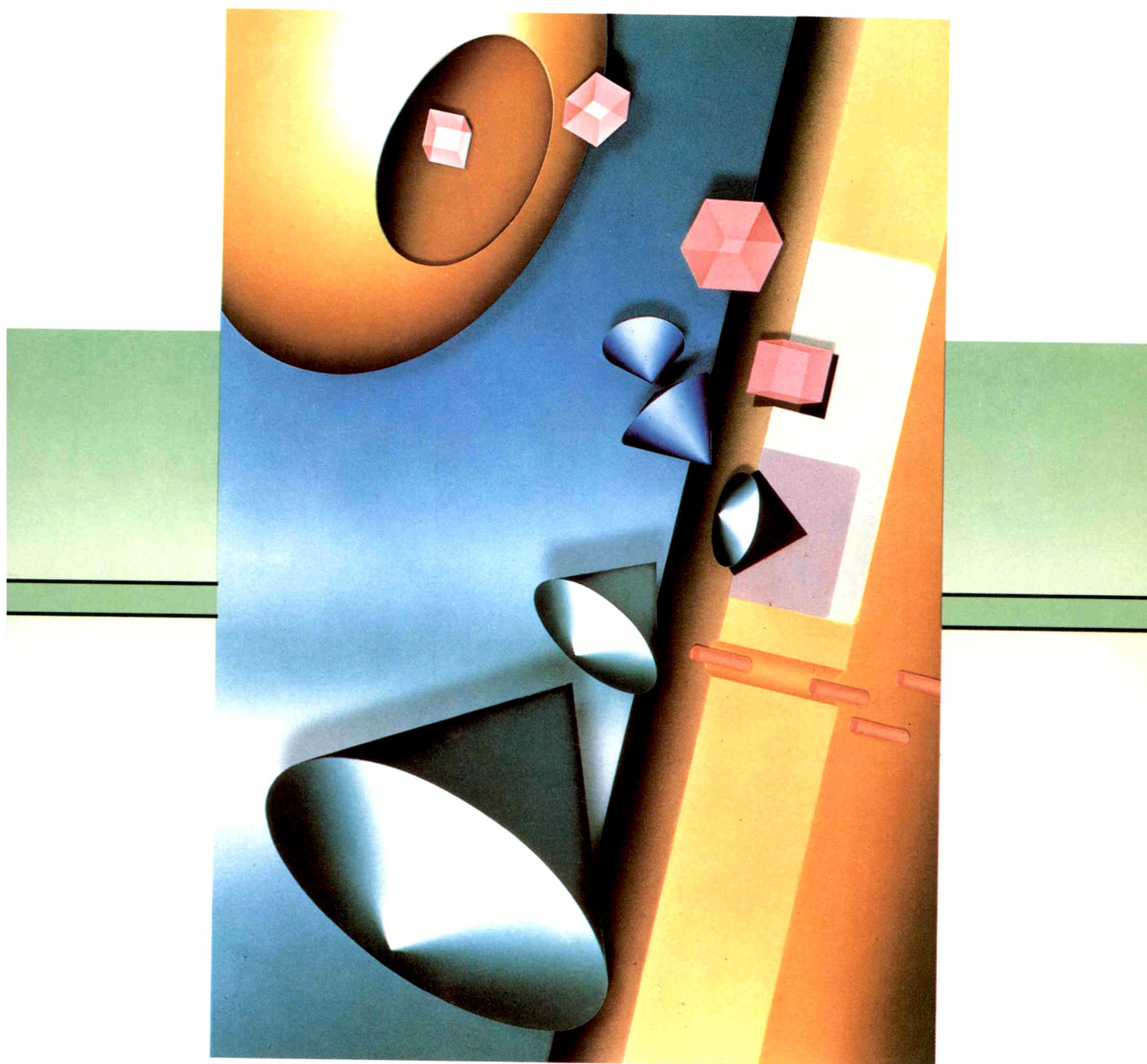
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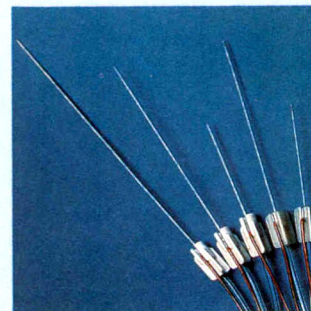
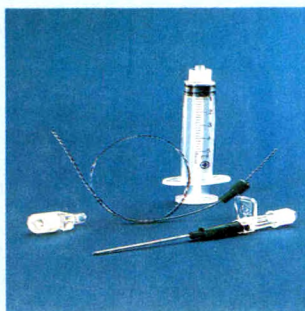
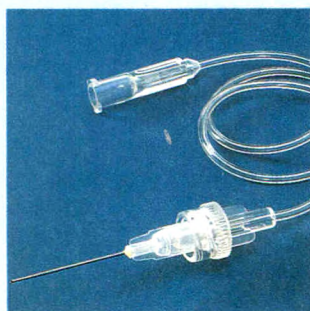
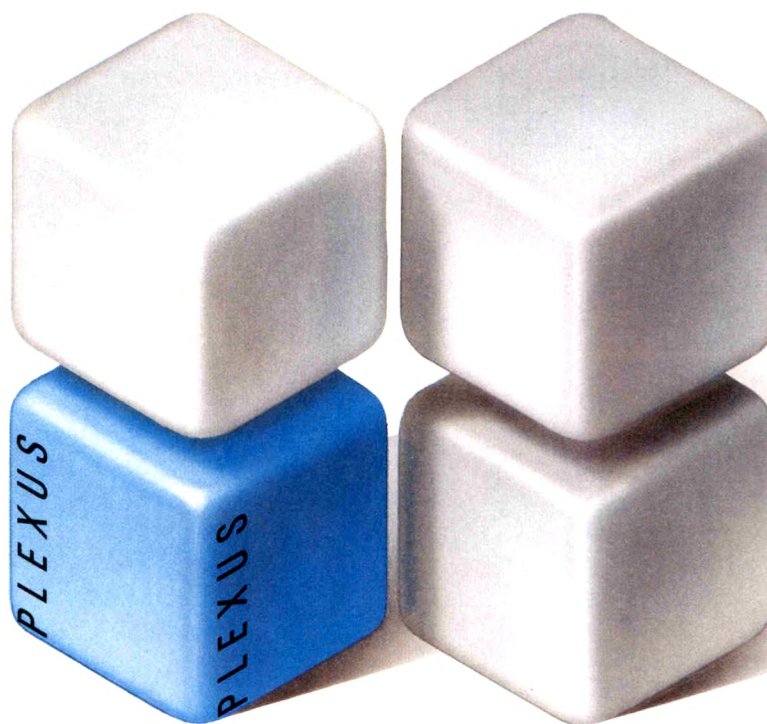
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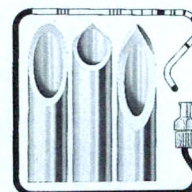


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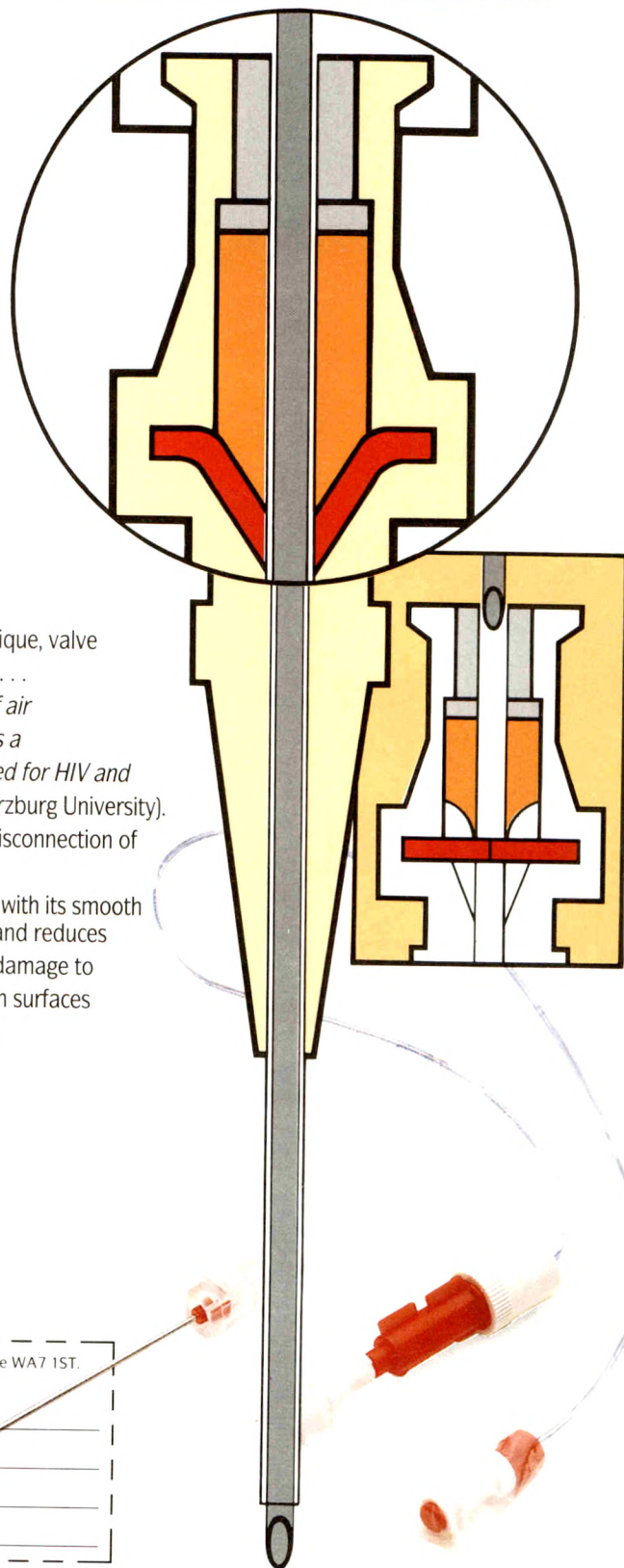
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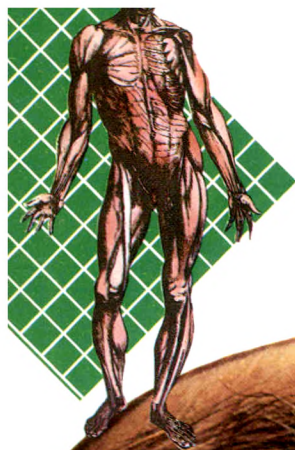
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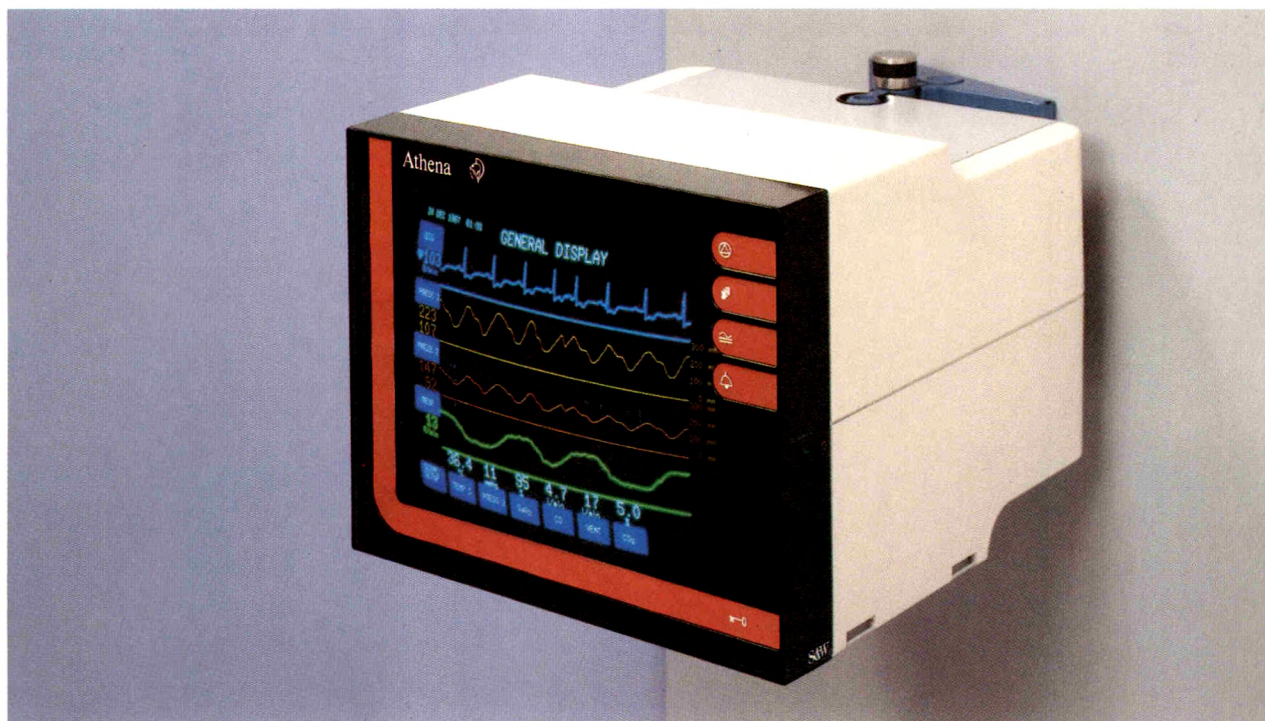
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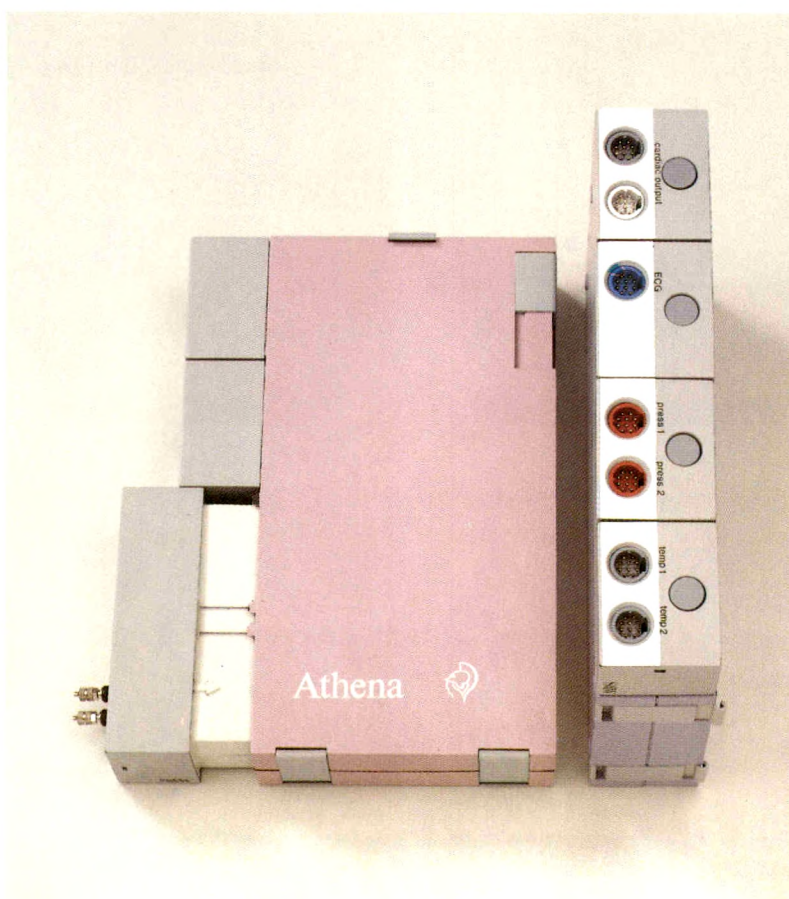
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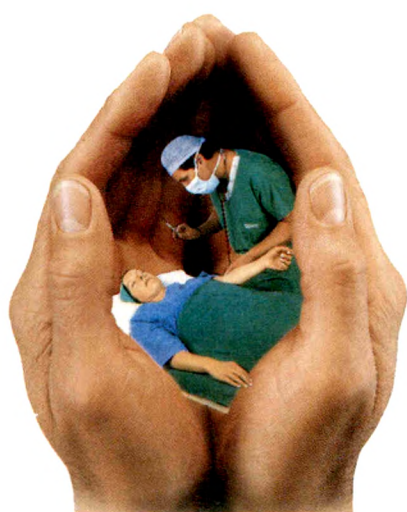
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Effects of beta-adrenoceptor antagonism on the cardiovascular and catecholamine responses to tracheal intubation

K. J. ACHOLA, M. J. JONES, R. W. D. MITCHELL AND G. SMITH

Summary

The catecholamine and cardiovascular responses to laryngoscopy and tracheal intubation were studied in 20 patients who underwent elective gynaecological surgery and who were allocated randomly to receive either practolol 10 mg or saline intravenously prior to induction of anaesthesia. Anaesthesia was induced with fentanyl and thiopentone; atracurium was administered and the lungs were ventilated artificially with 67% nitrous oxide in oxygen. Tracheal intubation was performed when muscle relaxation was adequate. Arterial pressure, heart rate, plasma noradrenaline and adrenaline concentrations were measured before and after tracheal intubation. A significant increase in catecholamine concentrations occurred in both groups in response to tracheal intubation but the magnitude of the increase in adrenaline was greater in the practolol group. There were no significant differences in arterial pressure or heart rate changes between the groups. We conclude that pretreatment with practolol is of no value in the attenuation of the hypertensive response to direct laryngoscopy and tracheal intubation in previously normotensive patients.

Key words

Intubation, tracheal; complications.

Sympathetic nervous system; catecholamines, sympatholytic agents, practolol.

The circulatory responses to direct laryngoscopy and tracheal intubation and the associated changes in plasma catecholamines are well recognised.^{1,2} Numerous methods have been used in an attempt to attenuate these responses^{3,4} but no single technique has gained widespread acceptance.

Many authorities advocate the use of beta-adrenoceptor antagonists to inhibit the reflex sympatho-adrenal discharges which follow tracheal intubation.^{5,6} It is recommended that patients who already receive beta-adrenoceptor antagonists in the treatment of cardiovascular disease should continue to do so up to the time of surgery. However, the use of such agents immediately before induction of anaesthesia in patients who have not previously taken these drugs is controversial. Prys-Roberts⁵ used practolol in hypertensive subjects and found it to attenuate significantly the tachycardia and hypertensive response after laryngoscopy and tracheal intubation. Similarly, Coleman and Jordan⁷ reported only a small increase in systolic arterial pressure in patients who received metoprolol. However, other investigators⁸ have failed to modify the hypertensive response to laryngoscopy with practolol, or have recorded deleterious cardiovascular effects.⁹

The authors are unaware of any study in which sympatho-adrenal activity, as assessed by measurement of plasma

catecholamines, was investigated when beta-adrenoceptor antagonists were administered during induction of anaesthesia. The present study was designed, therefore, to compare the cardiovascular and catecholamine responses with or without practolol, a selective beta₁ antagonist, during induction of anaesthesia and tracheal intubation.

Methods

Twenty otherwise healthy women about to undergo elective gynaecological surgery and who required tracheal intubation, gave informed consent for the study, which was approved by the District Ethical Committee. The patients were allocated randomly to receive either practolol 10 mg or placebo (saline 0.9%) before tracheal intubation.

Premedication consisted of diazepam 10 mg orally 1–2 hours before operation. In the anaesthetic room a 16-gauge cannula was placed in a vein in the antecubital fossa after local intradermal injection of plain lignocaine 0.5%. An automatic arterial pressure cuff (Copal) was placed on the contralateral arm and electrocardiogram (ECG) electrodes attached to record standard limb lead II. Baseline readings of arterial pressure and heart rate were recorded after a stabilisation period of 5 minutes and a 10-ml sample of

K.J. Achola, Msc, Chief Technician, M.J. Jones, BSc, MRCP, FFARCS, Lecturer, R.W.D Mitchell, BSc, FFARCS, Senior Registrar, G. Smith, BSc, MD, FFARCS, Professor, University Department of Anaesthesia, Leicester Royal Infirmary, Leicester LE1 5WW.

Accepted 10 November 1987.

venous blood aspirated from the cannula for baseline measurements of plasma noradrenaline and adrenaline concentrations.

Patients then received either practolol 10 mg in a volume of 5 ml or an equal volume of saline 0.9% injected slowly through the cannula over a one-minute period. Continuous ECG monitoring was performed throughout this period. Further arterial pressure and heart rate were recorded one minute after injection, and blood taken for catecholamine assay.

Anaesthesia was induced with fentanyl 0.1 mg followed by a dose of thiopentone 3–4 mg/kg sufficient to induce sleep; atracurium 0.4 mg/kg was administered to facilitate tracheal intubation. Anaesthesia was maintained with 67% nitrous oxide in oxygen with artificial ventilation of the lungs with a Bain breathing system and a fresh gas flow of approximately 90 ml/kg.

Further venous blood samples were obtained one minute after induction (assessed by loss of eyelash reflex) and 1, 3 and 5 minutes after intubation. Heart rate and arterial pressure were also recorded at these times.

The 10-ml blood samples were collected into lithium heparin tubes and centrifuged as soon as possible. The separated plasma was analysed for noradrenaline and adrenaline concentrations with a high-pressure liquid chromatographic technique. This method was described originally by Keller and colleagues¹⁰ for tissue catecholamine measurements and was adapted in our laboratory.¹

Data were analysed with the unpaired Student's *t*-test.

Results

There were no significant differences between the groups in age and weight (Table 1). Mean systolic arterial pressures before induction were similar in both groups (Fig. 1). No change occurred after the injection of practolol or saline in

either group. Systolic arterial pressure decreased by approximately 21% and 10% after induction of anaesthesia in the practolol and placebo groups, respectively (both $p < 0.001$). However, systolic arterial pressure one minute after tracheal intubation increased significantly ($p < 0.05$) above baseline levels in both groups to a similar extent (approximately 13%). Systolic arterial pressure 5 minutes after intubation decreased below baseline levels in the practolol group ($p < 0.01$).

Mean diastolic pressure remained unchanged after practolol or saline was injected (Fig. 1). Diastolic arterial pressure one minute after induction of anaesthesia decreased significantly ($p < 0.05$) below pre-induction values in the practolol group, whilst there was no change in the placebo group. However, the increases above baseline levels in the practolol and placebo groups one minute after tracheal intubation, were similar at 27% and 20% respectively (both $p < 0.001$). Diastolic arterial pressure 5 minutes after intubation returned to baseline levels in both groups.

Mean heart rate was slightly higher in the placebo group before induction (Fig. 2). Heart rate decreased by approximately 10% from baseline levels after administration of practolol. The increase in heart rate after tracheal intubation was similar in both groups and no significant intergroup difference was apparent.

Baseline mean (SEM) plasma noradrenaline concentrations were 1.70 (0.14) and 2.57 (0.37) pmol/ml in the placebo and practolol groups, respectively. No change in noradrenaline concentrations occurred after administration of either placebo or practolol, while induction of anaesthesia resulted in a decrease in both groups. Plasma noradrenaline increased significantly above baseline concentrations one minute after tracheal intubation in both the practolol and placebo groups. Analysis of data expressed as the percentage change from baseline concentrations, revealed no significant intergroup differences.

Baseline adrenaline concentrations were similar and did not alter after either practolol or saline administration. However, adrenaline concentrations one minute after tracheal intubation increased significantly in the practolol group by approximately 82% ($p < 0.01$) above baseline concentrations compared to 10% ($p < 0.05$) in the saline

Table 1. Details of patients. Values expressed as mean (SEM).

Group	Age, years	Weight, kg
Practolol	34 (2.0)	62 (3.0)
Placebo	29 (2.0)	62 (3.0)

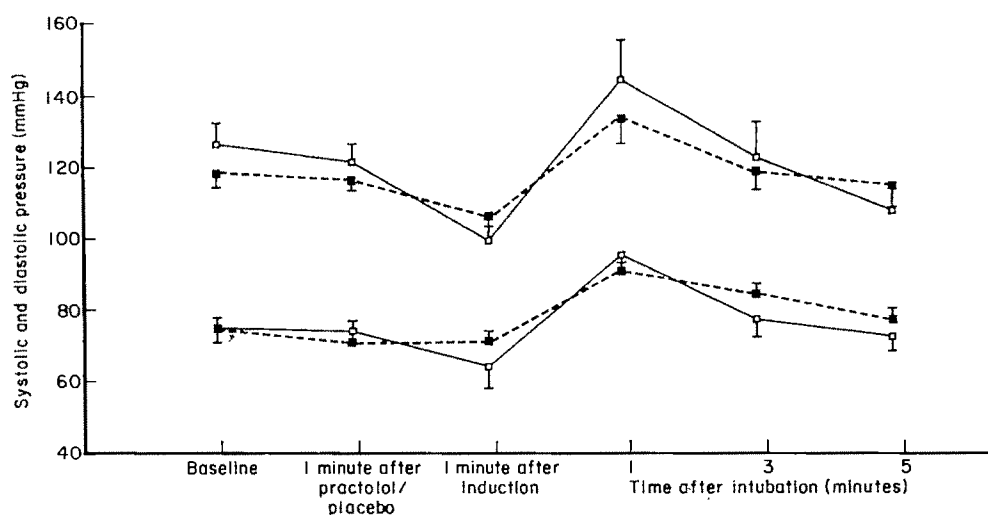


Fig. 1. Mean (SEM) systolic and diastolic arterial pressures in both groups during the study. $n = 10$ in each group. ■, placebo; □, practolol.

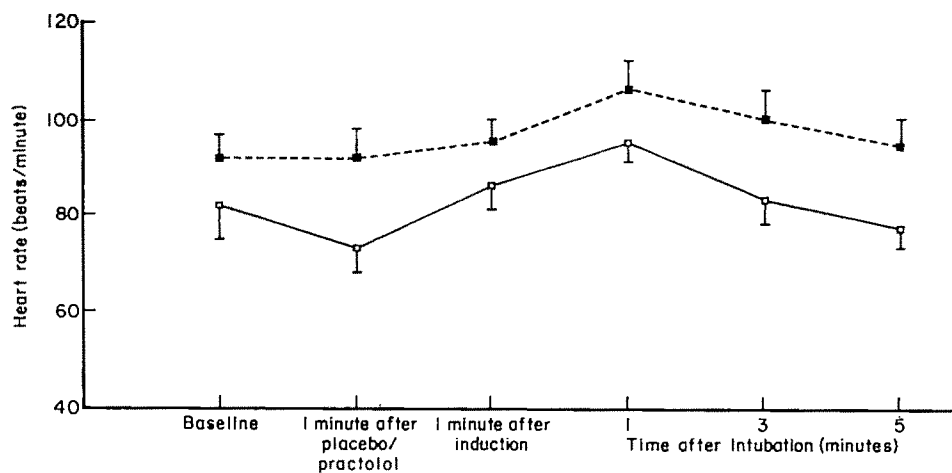


Fig. 2. Mean (SEM) heart rates in both groups during the study. $n = 10$ in each group. ■, placebo; □, practolol.

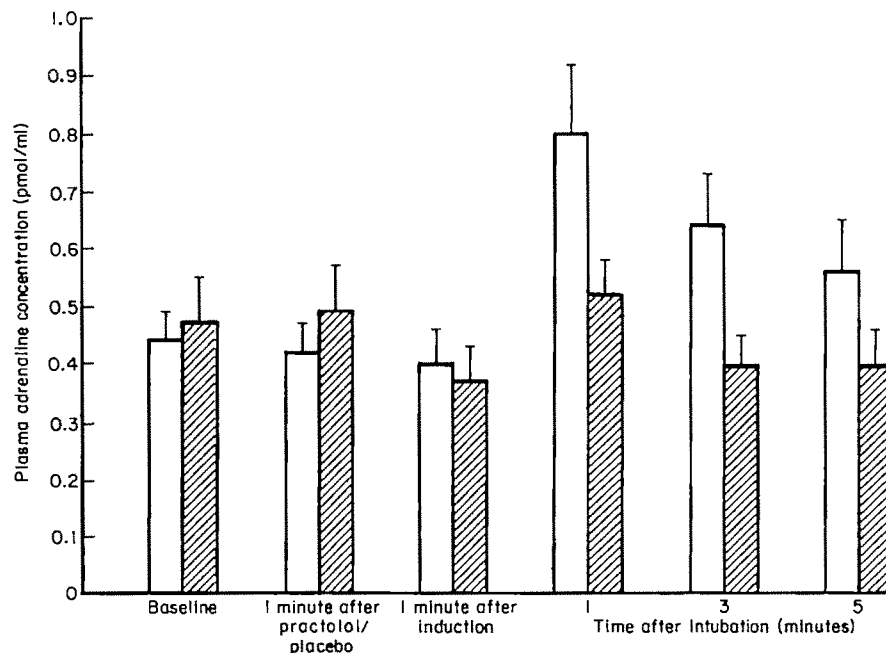


Fig. 3. Mean (SEM) Plasma adrenaline concentrations in both groups during the study. $n = 10$ in each group. □, practolol; ■, placebo.

group (Fig. 3). Adrenaline concentrations between groups were significantly different ($p < 0.05$) at one and three minutes after tracheal intubation. Plasma adrenaline concentrations remained elevated in the practolol group at five minutes after intubation.

Discussion

This study failed to demonstrate any attenuation of the hypertensive response to laryngoscopy and tracheal intubation by administration of practolol 10 mg intravenously immediately before induction of anaesthesia. Furthermore, beta-adrenoceptor antagonism with practolol did not prevent tachycardia during induction of anaesthesia and subsequent tracheal intubation.

The findings confirm the results of Werner *et al.*⁸ but are

at variance with those of Prys-Roberts *et al.*⁵ However, there are important differences in design between this latter study and the present one. Prys-Roberts studied hypertensive patients who were taking regular antihypertensive therapy; practolol 0.4 mg/kg was administered during nitrous oxide/halothane anaesthesia. The myocardial depression from halothane may have been potentiated by this large dose of practolol, and may have minimised the pressure response to tracheal intubation. Turner *et al.*¹¹ confirmed that such patients do not become hypertensive after intubation, because halothane decreases arterial pressure before intubation.

Previous studies¹ show a significant correlation between mean arterial pressure and increases in plasma nor-adrenaline concentrations. It would be surprising, therefore, if the use of beta-adrenoceptor antagonism alone

successfully inhibited the hypertensive response to tracheal intubation without the concomitant use of alpha-adrenoceptor blockade.

The present study demonstrated no significant differences in noradrenaline concentrations after tracheal intubation between patients given practolol and those given placebo. However, adrenaline concentrations were significantly higher in the practolol group one and 3 minutes after tracheal intubation ($p < 0.05$). Britton *et al*¹² demonstrated a significant increase in plasma adrenaline concentrations in a study of the effects of beta-adrenoceptor antagonism on the plasma adrenaline response to exercise. These findings differ from other reports¹³ among patients pretreated with metoprolol for 4 days before anaesthesia for microlaryngoscopy, in whom mean noradrenaline concentrations were almost twice as great as those in controls but adrenaline concentrations were unchanged. The explanation of these exaggerated noradrenaline responses is obscure but they may be a consequence of delayed removal of catecholamines from plasma in the presence of beta-adrenoceptor antagonists after several days of pretreatment. Long-term administration of propranolol is known to reduce plasma noradrenaline clearance by approximately 20%.¹⁴ Diminished hepatic extraction of noradrenaline as a result of reduced cardiac output is one possible mechanism of reduced noradrenaline clearance. Inhibition of the enzymes responsible for the degradation of catecholamines is another untested possibility.

Both metoprolol and practolol are cardioselective beta-adrenoceptor antagonists but only the latter possesses partial agonist or intrinsic sympathomimetic activity. Drugs with intrinsic activity would be expected to reduce resting heart rate less than those without it. It is interesting to speculate that the increase in plasma adrenaline concentrations which followed administration of practolol may be responsible for its partial agonist effect. The unchanged adrenaline levels with metoprolol in the absence of intrinsic sympathomimetic activity support such a hypothesis.

Our conclusions are therefore that the institution of beta-adrenoceptor antagonism with practolol shortly before anaesthesia does not effectively counteract the hypertensive response to laryngoscopy and tracheal intubation. Plasma adrenaline concentration in response to these stimuli was increased in the presence of beta-adrenoceptor antagonists

but no alteration in noradrenaline concentration was found.

References

1. DERBYSHIRE DR, CHMIELEWSKI A, FELL D, VATER M, ACHOLA KJ, SMITH G. Plasma catecholamine responses to tracheal intubation. *British Journal of Anaesthesia* 1983; **55**: 855-9.
2. SHRIBMAN AJ, SMITH G, ACHOLA AJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. *British Journal of Anaesthesia* 1987; **50**: 295-9.
3. DERBYSHIRE DR, SMITH G. Sympathoadrenal responses to anaesthesia and surgery. *British Journal of Anaesthesia* 1984; **56**: 725-39.
4. DERBYSHIRE DR, SMITH G, ACHOLA KJ. Effect of topical lignocaine on the sympathoadrenal responses to tracheal intubation. *British Journal of Anaesthesia* 1987; **59**: 300-4.
5. PRYS-ROBERTS C, FOEX P, BIRO GP, ROBERTS JG. Studies of anaesthesia in relation to hypertension. V. Adrenergic beta-receptor blockade. *British Journal of Anaesthesia* 1973; **45**: 671-80.
6. LOW JM, HARVEY JT, PRYS-ROBERTS C, DAGNINO J. Studies of anaesthesia in relation to hypertension. VII. Adrenergic responses to laryngoscopy. *British Journal of Anaesthesia* 1986; **58**: 471-7.
7. COLEMAN AJ, JORDAN C. Cardiovascular responses to anaesthesia. Influence of beta-adrenoceptor blockade with metoprolol. *Anaesthesia* 1980; **35**: 972-8.
8. WERNER O, MAGNUSSON J, FLETCHER R, NILSSON-EHLE P, PAHL M O. I.V. practolol during microlaryngoscopy. Effect on arterial pressure, heart rate, blood glucose and lipolysis. *British Journal of Anaesthesia* 1980; **52**: 91-6.
9. FARNON D, CURRAN J. Beta-receptor blockade and tracheal intubation. *Anaesthesia* 1981; **36**: 803-5.
10. KELLER R, OKE A, MEFFORD I, ADAMS RN. Liquid chromatographic analysis of catecholamines routine assay for brain mapping. *Life Science* 1976; **19**: 995-1003.
11. TURNER DAB, SHRIBMAN AJ, SMITH G, ACHOLA KJ. Effect of halothane on cardiovascular and plasma catecholamine responses to tracheal intubation. *British Journal of Anaesthesia* 1986; **58**: 1365-70.
12. BRITTON BJ, HAWKEY C, WOOD WG, PEELE M. Stress—a significant factor in venous thrombosis? *British Journal of Surgery* 1974; **61**: 814-20.
13. MAGNUSSON J, WERNER O, CARLSSON C, NORDEN N, PETTERSSON KI. Metoprolol, fentanyl and stress responses to microlaryngoscopy. Effects on arterial pressure, heart rate and plasma concentrations of catecholamines, ACTH and cortisol. *British Journal of Anaesthesia* 1983; **55**: 405-13.
14. ESLER M, JACKMAN G, LEONARD P, SKEWS H, BOBIK A, JENNINGS G. Effect of propranolol on noradrenaline kinetics in patients with essential hypertension. *British Journal of Clinical Pharmacology* 1981; **12**: 375-80.

Successful difficult intubation

Use of the gum elastic bougie

J. F. KIDD, A. DYSON AND I. P. LATTO

Summary

The reliability of two signs of tracheal placement of a gum elastic bougie was studied. These signs were clicks (produced as the tip of the bougie runs over the tracheal cartilages) and hold up of the bougie as it is advanced (when the tip reaches the small bronchi). Ninety-eight simulated and two genuine Grade 3 difficult intubations were attempted with the aid of a gum elastic bougie. Seventy-eight tracheal and 22 oesophageal placements of the bougie resulted. No clicks or hold up occurred with the bougie in the oesophagus. Clicks were recorded in 89.7% of tracheal placements of the bougie. Hold up at between 24–40 cm occurred in all tracheal placements. We conclude that these signs are reliable and that they should be taught as part of any difficult intubation drill in which the gum elastic bougie is used.

Key words

Intubation, tracheal; difficult.

Difficulties in tracheal intubation occur infrequently and are often unforeseen.^{1–5} Mismanagement may prove disastrous.^{6–7} The gum elastic bougie is a favourite aid used by British anaesthetists⁴ and was described by Macintosh in 1949.⁸ Successful tracheal intubation with the bougie involves two phases: placement of the bougie in the trachea, and threading the tracheal tube over the bougie down into the trachea.

Sellers and Jones⁹ suggest that tracheal placement of the bougie may be ascertained in three ways. Firstly, the tracheal rings may be felt as the bougie slides in (henceforth referred to as clicks). Secondly, the bougie may be held up as the small bronchi are reached whereas, if it is in the oesophagus, the whole length of the bougie may be inserted. Thirdly the patient may cough. This last sign is less helpful since in many instances the patient is paralysed with muscle relaxants. These signs have not previously been studied systematically.

This study was designed to test the reliability of tracheal clicks and hold up as signs of tracheal placement of the gum elastic bougie.

Methods

Ethical committee approval was obtained. One hundred patients in ASA grades 1 and 2 who were to have tracheal intubation performed during anaesthesia for elective surgery were studied. Difficulty in visualisation of the glottis was not anticipated. Intubations were performed by three anaesthetists each with between 5 and 8 years in the specialty.

Patients were pre-oxygenated for 3 minutes, anaes-

thesia induced intravenously and a muscle relaxant administered. No cricoid pressure was applied. Laryngoscopy was performed when judged clinically appropriate with a size three or four Macintosh blade and this view of the glottis was recorded according to a previously published classification.² *Grade 1:* Glottis (including anterior and posterior commissures) can be fully exposed. *Grade 2:* Glottis can be partly exposed (posterior commissure only). *Grade 3:* Glottis cannot be exposed (only epiglottis visualised). *Grade 4:* Neither glottis nor epiglottis can be exposed.

Difficult intubation was then simulated as described by Cormack and Lehane by allowing the epiglottis to fall so as to obscure the cords, to convert a grade 1 view into a grade 3 view.²

A 13 FG 60-cm gum elastic bougie (Eschmann, England) marked at 5-cm intervals was then inserted posterior to the epiglottis. The bougie was advanced and the number of clicks produced by the tip of the bougie running over the tracheal cartilages recorded. The bougie was then further advanced until either resistance was encountered, in which case the length inserted measured at the lips was recorded, or all 60 cm inserted.

The anaesthetist then revealed a full view of the glottis and the presence of the bougie in either the trachea or the oesophagus was noted. If the bougie was in the oesophagus it was removed and the trachea intubated normally. If the bougie was in the trachea a grade 3 view of the glottis was re-established and the laryngoscope held in this position. Then a Portex standard cuffed tracheal tube of either 9-mm internal diameter for men or 8-mm for women was

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Table 1. Incidence of clicks and hold up according to bougie placement.

	Oesophagus (n = 22)		Trachea (n = 78)	
	clicks	hold up	clicks	hold up
Present	0	0	70 (89.7%)	78 (100%)
Absent	22 (100%)	22 (100%)	8 (10.3%)	0

threaded over the gum elastic bougie into the trachea. The procedure was abandoned and the trachea intubated normally if this was unsuccessful.

Results

One hundred adults were studied, 49 men and 51 women. The initial views at laryngoscopy were Grade 1: 82 patients, Grade 2: 15, Grade 3: 2 and Grade 4: 0. That is two patients were truly difficult intubations.

The bougie was found to have been placed in the trachea on 78 occasions and in the oesophagus in 22 (see Table 1). Of the 78 tracheal placements of the bougie, clicks were present in 70 (89.7%) with a mean of 3.7 clicks (range 1–6, mode 4, SD 1.18). Hold up of the bougie occurred in all 78 tracheal placements (100%) at a mean distance of 31.9 cm (range 24–40, SD 3.68) from the lips. In none of the 22 oesophageal placements were clicks or hold up recorded on advancement of the bougie.

Discussion

The suggestion that clicks due to the movement of the tip of the bougie over the tracheal cartilages, and hold up as the tip reaches the small bronchi are reliable signs of placement of the bougie in the trachea is supported.

Clicks were recorded in all but 10.3% of tracheal placements of the bougie; these were either of insufficient strength to be detected by the anaesthetist, or absent due to the movement of the tip of the bougie down the lumen but which did not touch the wall and cartilages of the trachea. More extreme concave anterior curvature of the bougie may elicit a higher rate of click detection but the possibility of false negatives remains. Hold up occurred in all 100% of tracheal placements of the bougie. It must be emphasised that excessive force to advance the bougie should be avoided because damage to, or even rupture of, a bronchus could result.

Neither of these signs was elicited in any of the oesophageal placements of the bougie. It is possible that oesophageal stenosis could result in hold up of the 13 FG gum elastic bougie but would have to be so severe as to cause unmistakable symptoms before operation. Cricoid pressure could similarly cause hold up in the oesophagus but would be at such a distance that the bougie could not possibly have reached the small bronchi.

Therefore, a logical routine for the use of the gum elastic bougie during a difficult intubation is as follows. Insert the bougie and if clicks are felt, proceed with intubation. If

clicks are not felt the bougie should be carefully advanced to a maximum distance of 45 cm. Proceed with intubation if hold up occurs. The bougie is in the oesophagus and should be removed if clicks are not felt and hold up does not occur. Another attempt to insert the bougie into the trachea may be made or an alternative stratagem employed. However, we still consider it essential to confirm successful tracheal intubation even if one or both signs are unequivocally present and the tracheal tube is easily threaded over the bougie. This is best done by capnography.

The occurrence of two genuine Grade 3 views of the glottis on initial laryngoscopy of 100 nonobstetric patients was unexpectedly high. This may have been due to chance given the small sample population of 100 patients or may be an accurate reflection of the true incidence. Cormack and Lehane estimate the frequency of Grade 3 difficult intubations at 1:2000.² Others who examined difficult intubation but who did not systematically grade glottic views as above reported an incidence of 1% (Cardiff Anaesthetic Record System 1972–1979, population 109 000), 2.3% (population 3482)¹ and 3.4% (population 1200).⁴ Samsoon and Young examined failed intubation retrospectively and reported an incidence of 1:280 (population 1980) for obstetric patients and 1:2230 (population 13 380) for nonobstetric patients, most of whom had Grade 3 views at laryngoscopy.⁵ However, some successful intubations in these groups may have been difficult. A large prospective study in obstetric and nonobstetric patients is required to estimate the actual incidence of Grade 3 difficult intubation.

In conclusion we recommend that detection of tracheal clicks and hold up of the bougie be taught as an essential part of a difficult intubation drill that utilises the gum elastic bougie. The bougie should be removed and re-inserted or an alternative technique applied if no clicks are elicited or no hold up occurs on its advancement. To attempt intubation in the absence of these signs will almost certainly result in oesophageal intubation, waste valuable time and expose the patient to needless additional risk.

References

1. ARO L, TAKKI S, AROMAA U. Technique for difficult intubation. *British Journal of Anaesthesia* 1971; **43**: 1081–3.
2. CORMACK RS, LEHANE J. Difficult tracheal intubation in obstetrics. *Anaesthesia* 1984; **39**: 1105–11.
3. LYONS G. Failed intubation. Six years' experience in a teaching maternity unit. *Anaesthesia* 1985; **40**: 759–62.
4. LATTO IP. Management of difficult intubation. In: LATTO IP, ROSEN M, eds. *Difficulties in tracheal intubation*. Eastbourne: Ballière Tindall/W.B. Saunders, 1985: 99–141.
5. SAMSOON GLT, YOUNG JRB. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987; **42**: 487–90.
6. LUNN JN, MUSHIN WW. *Mortality associated with anaesthesia*. London: Nuffield Provincial Hospitals Trust, 1982.
7. *Report on confidential enquiries into maternal deaths in England and Wales 1979–1981*. London: Her Majesty's Stationery Office, 1986.
8. MACINTOSH RR. An aid to oral intubation. *British Medical Journal* 1949; **1**: 28.
9. SELLERS WFS, JONES GW. Difficult tracheal intubation. *Anaesthesia* 1986; **41**: 93.

Plasma lignocaine levels during paediatric endoscopy of the upper respiratory tract

Relationship with mucosal moistness

H. B. WHITTET, A. W. HAYWARD AND E. BATTERSBY

Summary

Plasma lignocaine levels were measured at 5, 10 and 15 minutes following local application (4 mg/kg) to the upper airway in children who underwent endoscopy under general anaesthesia. These levels were then correlated with the appearance of the moistness of the airway mucosa secondary to premedication with atropine. This latter assessment was carried out by one anaesthetist who used a predetermined scale of 1–5, where 1 was very dry and 5 very wet. Significantly higher ($p < 0.05$) plasma levels of lignocaine were achieved when the mucosa was 'very dry' especially in children under 2 years of age. The total dose of lignocaine applied to the upper airway of children should probably be reduced, in the presence of a 'dry' mucosa after effective antisialogogue premedication, and especially when less than 2 years of age.

Key words

*Anaesthetics, local; lignocaine.
Premedication; atropine.*

Anaesthesia for routine endoscopy of the upper airway in children at Great Ormond Street Hospital involves the use of a spontaneous ventilation technique with local application of lignocaine to inhibit the laryngeal reflexes. Previous studies^{1–4} have shown that high plasma levels of local anaesthetics may be achieved from topical absorption. The rate of absorption is thought to be related to the moistness of the mucosa of the upper airway and hence the efficacy of the premedication as an antisialogogue.

The purpose of this study was to correlate the plasma levels of lignocaine, following local application to the upper airway, to the moistness of the mucosa.

Methods

Thirty children were studied, with ages which ranged from 8 months to 10 years, and weights from 7–24 kg. They had all been referred to hospital for assessment of congenital and acquired upper airway abnormalities and were otherwise healthy. Informed consent for the study was obtained from the parents.

All patients were premedicated with intramuscular atropine 0.02 mg/kg, one hour pre-operatively. Anaesthesia was induced with either cyclopropane in oxygen or halothane in nitrous oxide and oxygen. A 23-gauge winged needle was put into a vein in the antecubital fossa and suxamethonium 1 mg/kg was administered once anaesthesia was achieved.

Laryngoscopy was performed by a consultant anaesthetist, after manual inflation of the lungs via a facemask with 100% oxygen, and a subjective assessment made of the degree of moistness of the upper airway mucosa using a previously agreed 1–5 scale. On this scale, 1 was taken to represent a very dry mucosa; 2 a dry mucosa; 3 a moist mucosa; 4 a wet mucosa; and 5 a very wet mucosa.

The anaesthetist then sprayed the upper airway with lignocaine via a metered spray; each spray delivered 10 mg of lignocaine base. A dose of 4 mg/kg was directed in equal proportions to the supraglottic, glottic and subglottic regions. The accuracy of this aerosol was verified by dissolving one spray into a known amount of normal saline and analysing this solution in the same way as the blood samples.

A nasotracheal tube was passed and connected to an Ayre's T-piece. Anaesthesia was maintained with the patient breathing spontaneously halothane, nitrous oxide and oxygen. The distal end of the tube was withdrawn into the pharynx for the surgical part of the procedure.

Serial venous blood samples were taken from the indwelling needle at 5, 10 and 15 minutes from application of the lignocaine. These samples were preserved in lithium heparin prior to analysis by high pressure liquid chromatography.⁵ Blood was also taken for estimation of urea and electrolytes and liver function tests. The blood pressure and electrocardiograph were recorded throughout the procedure.

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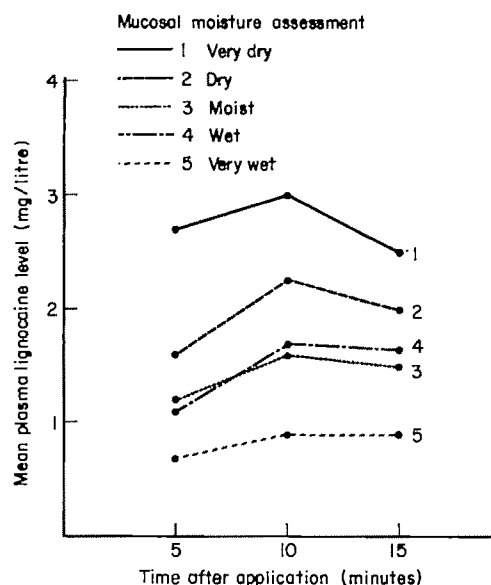


Fig. 1. Mean plasma lignocaine levels related to mucosal moisture assessment 5, 10 and 15 minutes after application.

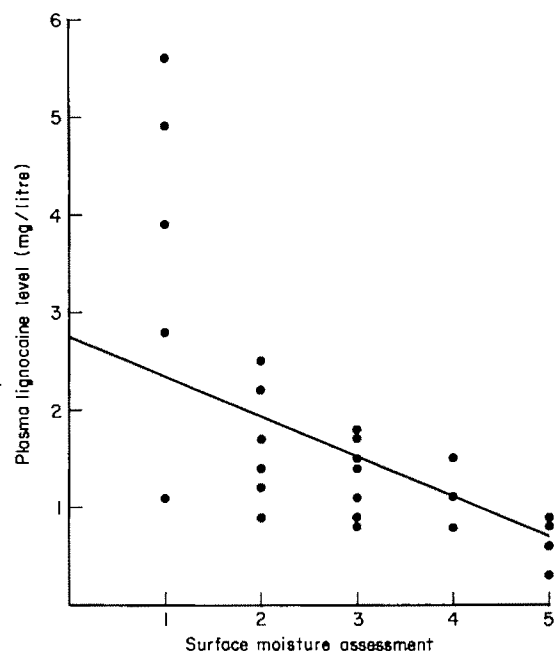


Fig. 2. Plasma lignocaine levels 5 minutes after application. ($n = 25$, $t = -2.07$, $R^2 = 15.9\%$, $p < 0.05$).

Statistical analysis was performed using a Statsgraphic package on an IBM ATe computer.

Results

A total of 30 patients were included in this study. Only 25 of these were able to have plasma estimations performed at all three time intervals, because of the short duration of the endoscopic procedure.

A multivariate regression analysis was performed to investigate possible influences upon plasma levels obtained. Moistness of mucosa, age, total dose of lignocaine, liver function tests, and urea and electrolytes were compared with plasma levels of lignocaine at 5, 10 and 15 minutes after application.

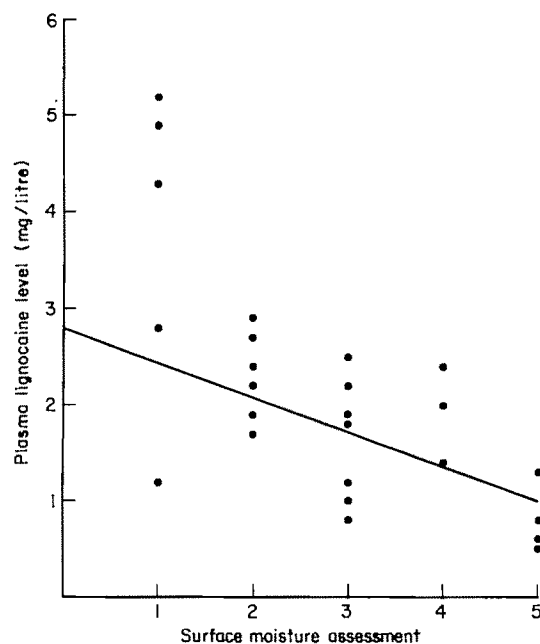


Fig. 3. Plasma lignocaine levels 10 minutes after application. ($n = 25$, $t = -2.25$, $R^2 = 16.0\%$, $p < 0.05$).

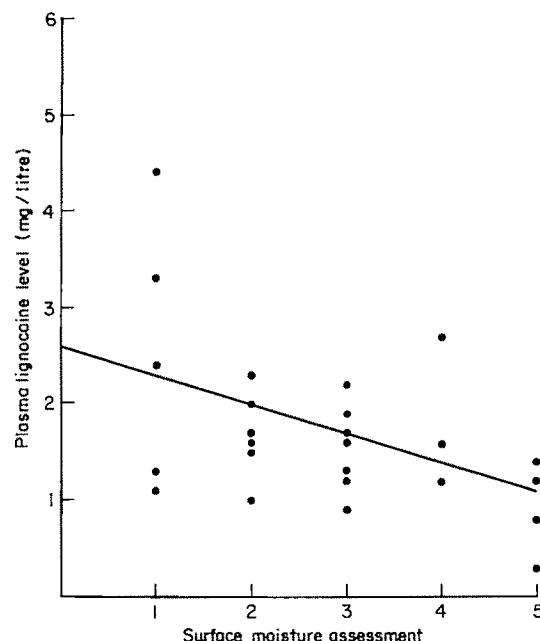


Fig. 4. Plasma lignocaine levels 15 minutes after application. ($n = 25$, $t = -2.05$, $R^2 = 15.7\%$, $p < 0.05$).

Of these factors only mucosal moistness of the upper airway showed a significant, but inverse, correlation with the plasma levels of lignocaine. Figure 1 shows the relationship between mucosal moisture assessment and mean plasma lignocaine levels attained for the three time intervals. Figures 2, 3, and 4 display the regression analysis best-fit lines for the actual plasma levels reached 5, 10 and 15 minutes after application. Analysis of variance produced an R-squared value of 16% for the full regression at each time interval. These values were statistically significant at all the time intervals with $p < 0.05$.

The relationship between age and plasma lignocaine levels was investigated further. Children under 2 years of age were found to have higher plasma levels than older

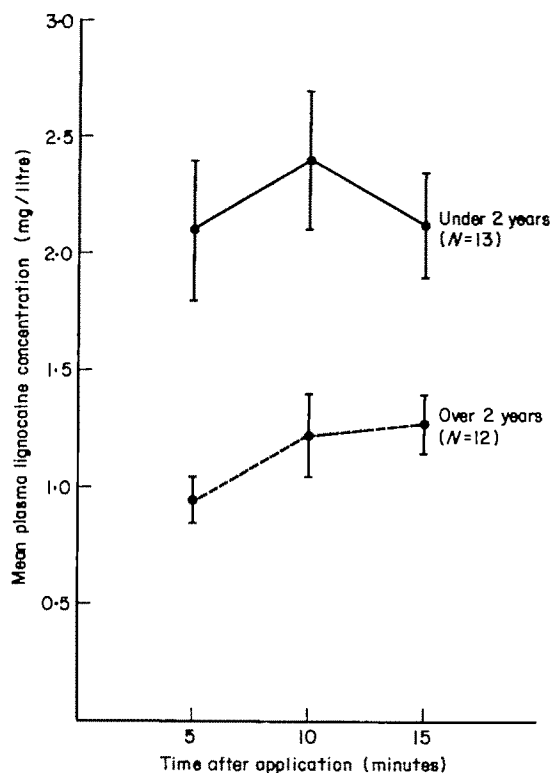


Fig. 5. Mean plasma lignocaine levels and age group.

children (see Fig. 5). These values were statistically significant at all time intervals ($p < 0.05$) using the unpaired Students *t*-test.

Discussion

Lignocaine is a widely used topical anaesthetic agent for endoscopic procedures of the upper respiratory tract. It is used alone as a local anaesthetic for adult fiberoptic bronchoscopy and oesophagoscopy and as an adjunct during paediatric upper airway endoscopy performed under general anaesthesia. The use of topical anaesthesia allows good surgical visualisation and assessment of the upper airway with a lighter plane of general anaesthesia, in this latter application.

Absorption from mucosal surfaces may be rapid and lead to high blood levels, although lignocaine is very effective as a surface anaesthetic. Many different factors influence the uptake or metabolism of lignocaine after local application. Factors which have been reported include droplet size of spray,⁶ site of spraying,⁷ loss of part of the solution through swallowing and exhalation in awake patients⁸ and the effect of renal and hepatic dysfunction on metabolism.⁹

To standardise this study we used an aerosol bottle which produced uniform droplet size (Xylocaine aerosol spray: Astra chemicals) and directed the spray in equal proportions to the supraglottic, glottic and subglottic areas. Adriani and Campbell¹⁷ have shown that absorption occurs more rapidly from the alveoli than other sites in the respiratory tract. All our patients were anaesthetised so that no local anaesthetic was swallowed or exhaled and serum urea and electrolytes and liver function tests were normal. The rate of uptake of lignocaine from the respiratory tract has been reported^{1,2,4,7} to range from 5–20 minutes. It was only possible to take blood samples for up to 15

minutes in our study, because of the shortness of the surgical procedure.

Atropine, with or without a sedative, is commonly used to premedicate children. It is mainly used for its vagolytic effect, although its antisialogogue action is also useful. However, it is less effective as a drying agent than hyoscine,¹⁰ and tends to vary more from patient to patient.

Our results show that significantly higher venous levels of lignocaine are achieved when the mucosa of the upper airway is dry. This is presumably mainly due to the saliva which can act as a barrier between the lignocaine and airway mucosa and may lead to a slower rate of uptake when the mucosa is wet. The pH of saliva following oral anticholinergic medication is quoted¹¹ as ranging from 7.19 to 7.32. Therefore there is unlikely to be a significant effect from change in pH on the absorption of lignocaine, whether the mucosa is wet or dry.

Eyres *et al.*¹² found that higher peak levels of lignocaine occurred in children under 3 years of age when compared with older children. Our results endorsed this finding in children less than 2 years of age and were statistically significant.

None of the children in our study showed any signs of systemic toxicity. The highest plasma level reached was 5.6 $\mu\text{g/ml}$ in a 6-month-old child 5 minutes after application of the lignocaine. The potentially toxic level in unanaesthetised adults is quoted as 5.3 $\mu\text{g/ml}$,¹³ whereas this level in anaesthetised adults is thought to be in the region of 10 $\mu\text{g/ml}$.¹⁴

In conclusion, topical lignocaine as an adjunct to general anaesthesia for upper airway assessment in children seems to be safe. However, in children under 2 years of age where the mucosal membranes are very dry, following efficient antisialogogue premedication, it may be sensible to reduce the total dose of lignocaine administered.

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References

1. PELTON DA, DALY M, COOPER PD, CONN AW. Plasma lidocaine concentrations following topical aerosol application to the trachea and bronchi. *Canadian Anaesthetists' Society Journal* 1970; **17**: 250–5.
2. CHU SS, RAH KH, BRANNAN MD, COHEN JL. Plasma concentration of lidocaine after endotracheal spray. *Anesthesia and Analgesia* 1975; **54**: 438–41.
3. CURRAN J, HAMILTON C, TAYLOR T. Topical analgesia before tracheal intubation. *Anaesthesia* 1975; **30**: 765–8.
4. SCOTT DB, LITTLEWOOD DG, COVINO BG, DRUMMOND GB. Plasma lignocaine concentrations following endotracheal spraying with an aerosol. *British Journal of Anaesthesia* 1976; **48**: 899–902.
5. HOLT DW, FLANAGAN RJ, HAYLER AM, LOIZOU M. Simple gas-liquid chromatographic method for the measurement of mexiletine and lignocaine in blood-plasma or serum. *Journal of Chromatography* 1979; **169**: 295–301.
6. CUSHING IE, MILLER WF. *Respiratory therapy*. Philadelphia: FA Davis Company, 1965: 173.

7. ADRIANI J, CAMPBELL D. Fatalities following topical application of local anesthetics to mucous membranes. *Journal of the American Medical Association* 1956; **162**: 1527-30.
8. TELIVUO L. An experimental study on the absorption of some local anaesthetics through the lower respiratory tract. *Acta Anaesthesiologica Scandinavica* 1965;(Suppl. 16): 121-126.
9. THOMSON PD, MELMON KL, RICHARDSON JA, COHN K, STEINBRUNN W, CUDIHIE R, ROWLAND M. Lidocaine pharmacokinetics in advanced heart failure, liver disease, and renal failure in humans. *Annals of Internal Medicine* 1973; **78**: 499-508.
10. WYANT GM, DOBKIN AB. Antisialogogue drugs in man. *Anaesthesia* 1957; **12**: 203-14.
11. PARVINEN T, PARVINEN I, LARMAS M. Stimulated salivary flow rate, pH and lactobacillus and yeast concentrations in medicated persons. *Scandinavian Journal of Dental Research* 1984; **92**: 524-32.
12. EYRES RL, KIDD J, OPPENHEIM R, BROWN TCK. Local anaesthetic plasma levels in children. *Anaesthesia and Intensive Care* 1978; **6**: 243-7.
13. FOLDES FF, MOLLOY R, McNALL PG, KOUKAL LR. Comparison of toxicity of intravenously given local anesthetic agents in man. *Journal of the American Medical Association* 1960; **172**: 1493-8.
14. BROMAGE PR, ROBSON JG. Concentrations of lignocaine in the blood after intravenous, intramuscular, epidural and endotracheal administration. *Anaesthesia* 1961; **16**: 461-78.

Reversal of pancuronium

Neuromuscular and cardiovascular effects of a mixture of neostigmine and glycopyrronium

D. R. GOLDHILL, P. B. EMBREE, H. H. ALI AND J. J. SAVARESE

Summary

Moderate to deep (67–99% single twitch depression) pancuronium-induced neuromuscular blockade was antagonised with neostigmine (30 µg/kg, 60 µg/kg, or 80 µg/kg) in combination with glycopyrronium. Twenty-seven patients were reversed from 91%–99% twitch depression. Recovery of the first twitch of a train-of-four to 95% of control twitch took at least 20 minutes with neostigmine 30 µg/kg. The higher doses were significantly faster (60 µg/kg $p < 0.05$, 80 µg/kg $p < 0.01$) and took 15.8 and 14.8 minutes respectively. Reversal to a train of four ratio of 0.75 was not consistently achieved in under 30 minutes with any dose of neostigmine.

Nineteen patients were antagonised from a 67%–80% depression of first twitch and in all but two recovery to 95% of control took under 10 minutes. To achieve a train of four ratio of 0.75 took less than 12.5 minutes except in three patients, two of whom, both given neostigmine 30 µg/kg, took longer than 20 minutes. Neostigmine 60 µg/kg produced as rapid a degree of antagonism as 80 µg/kg. Heart rates after reversal decreased gradually in all groups, although the decrease was initially greater in the low dose neostigmine (30 µg/kg) group. A fixed 5:1 ratio of neostigmine and glycopyrronium will usually antagonise a moderate (70%–80%) pancuronium block to a train of four of greater than 75% within 12.5 minutes if at least 60 µg/kg of neostigmine is administered. More than 30 minutes may be required for reversal whatever the dose of neostigmine, for antagonism from greater than 90% twitch depression.

Key words

Parasympathetic nervous system; glycopyrronium.
Antagonists, neuromuscular relaxants; neostigmine.

There are surprisingly few data concerning the optimum dose of neostigmine for a given level of blockade, although much has been written about antagonism of neuromuscular blockade. Many British anaesthetists use neostigmine 2.5 mg as their standard dose. Textbook advice on both sides of the Atlantic is to administer up to neostigmine 5 mg per 70 kg body weight.^{1,2} More is not usually recommended—too much antagonist may deepen rather than reverse blockade.³ To monitor with a train-of-four stimulator is useful to ascertain depth of paralysis, but to observe or feel the response may not provide sufficient information to determine accurately adequacy of reversal.⁴ Incomplete reversal may be common^{5,6} and is a potential cause of postoperative morbidity and mortality. It would certainly be helpful to know the optimum dose required when antagonism of neuromuscular blockade is attempted, especially from a deep level, and the expected time for the block to be fully counteracted. This study determines the dose of neostigmine and glycopyrronium required to antagonise a moderate to very deep pancuronium-induced neuromuscular blockade,

and provides information on the time that such reversal will take.

The combination of neostigmine and glycopyrronium has been shown to have an advantage over neostigmine and atropine for reversal of neuromuscular blockade.⁷ All our patients received a combination of neostigmine and glycopyrronium in a 1:5 mixture. The dose of neostigmine was varied from 30 µg/kg to 80 µg/kg which allowed us to examine the cardiovascular suitability of this mixture for reversal over the normal clinical range of dosage.

Methods

Ethical committee approval was obtained and verbal consent given by the patients who participated in the study. Fifty-one patients were studied. They were ASA 1 and 2, aged 18–65 years, weighed 45–111 kg and were to have elective surgery, during which the administration of muscle relaxants was appropriate. Drugs which would affect the neuromuscular junction, abnormal electrolytes, and any

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medication that might alter cardiac rhythm were specifically excluded.

Anaesthesia was induced with thiopentone (5–6 mg/kg) and maintained with nitrous oxide (66%) and supplements of morphine or fentanyl as indicated, after premedication with diazepam (0.1–0.2 mg/kg orally) and morphine (0.1–0.15 mg/kg intramuscularly). Ventilation of the lungs was controlled to maintain end tidal CO₂ of 4–5.3 kPa. Volatile agents were not used. The ulnar nerve was stimulated via needle electrodes at the wrist. Supramaximal train-of-four (TOF) stimuli of 0.2 ms duration at 2 Hz for 2 seconds were generated by a Grass S88 stimulator at a rate of 0.1 Hz. The hand and forearm were immobilised in a splint and the force of contraction of the adduction of the thumb was recorded through a Grass force displacement transducer on a Grass polygraph.

Pancuronium was administered in an initial dose of 0.08–0.1 mg/kg and increments were given to obtain a desired level of inhibition of the first twitch (T1) of the TOF response at reversal. Antagonism of residual block was accomplished by administration of a fixed ratio combination of neostigmine and glycopyrronium (1 ml = neostigmine 1 mg plus glycopyrronium 0.2 mg) given over one minute. Patients were allocated randomly to receive neostigmine with glycopyrronium, 30 µg/kg with 6 µg/kg (low dose), 60 µg/kg with 12 µg/kg (medium dose) or 80 µg/kg with 16 µg/kg (high dose).

Twenty seven of the first 32 patients were antagonised from a block of 91%–99% depression of T1 (very deep block), and three from 81%–90% depression of T1 (deep block). In two subjects no twitches were present at reversal and they are excluded from the neuromuscular analysis. Reversal from a moderate block, when T1 was between 67% and 80% of control twitch height (Tc), was evaluated in the remainder of 19 patients. Anaesthesia and neuromuscular monitoring were continued for 30 minutes in 24 of the patients with very deep blocks and at least 20 minutes in the other subjects. If a T4/T1 ratio of 0.75 had not been achieved by this time, patients were assessed clinically and given additional increments of antagonist as necessary.

The amplitude of the first twitch at reversal and the time to achieve a T1 of 95% of Tc and a TOF ratio of 0.75 were noted. The ECG was recorded continuously and blood pressure and heart rate taken prereversal and at 0,1,2,3,4,5,6,8,10,15 and 20 minutes postreversal. Results were compared by Anova and Student's *t*-test where appropriate.

Results

Neuromuscular data (Figs 1 and 2).

Very deep block (Table 1). Twenty-seven patients were reversed from 91% to 99% inhibition of T1 (nine patients in each reversal group). At least 20 minutes were required to reach a T1/Tc of 95% after administration of low dose neostigmine (30 µg/kg). The two higher doses of neostigmine achieved a T1/Tc of 95% significantly faster (60 µg/kg *p* < 0.05, 80 µg/kg *p* < 0.01) than neostigmine (30 µg/kg). None of the doses of neostigmine reliably produced a T4/T1 ratio of 0.75 within 30 minutes.

Moderate block (Table 2). In the 19 patients with an inhibition of T1 of 80% or less at reversal, recovery to a

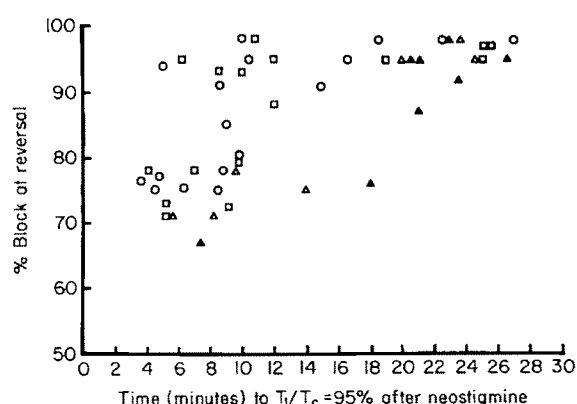


Fig. 1. Time after neostigmine to reach a T1/Tc of 95%. Δ , neostigmine 30 µg/kg; \square , neostigmine 60 µg/kg; \circ , neostigmine 80 µg/kg. \blacktriangle , longer than 30 minutes, when monitor period ended.

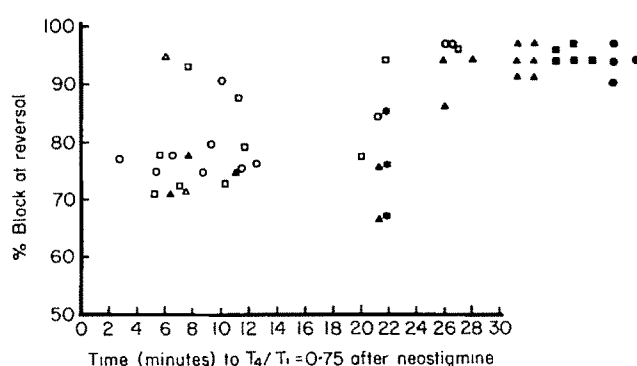


Fig. 2. Time after neostigmine to reach a T4/T1 ratio of 0.75. Δ , neostigmine 30 µg/kg; \square , neostigmine 60 µg/kg; \circ , neostigmine 80 µg/kg. \blacktriangle , \blacksquare , \bullet , longer than 30 minutes, when monitor period ended. \ast , longer than 20 minutes, when monitor period ended.

Table 1. Very deep block. Recovery indices for 3 doses of neostigmine, mean (SEM).

	Dose of neostigmine, glycopyrronium (µg/kg)		
	30/6 (low)	60/12 (medium)	80/16 (high)
<i>n</i>	9	9	9
% block of T1 at reversal	95.0 (0.7)	95.4 (0.6)	95.3 (1.0)
95% recovery of T1 (minutes)	<i>n</i> = 8 (A) 22.0 (0.8)	15.8 (2.5)*	14.8 (2.4)**
T4/T1 = 0.75 (minutes)	19.9 (<i>n</i> = 3) > 30 (<i>n</i> = 6)	18.8 (<i>n</i> = 3) > 30 (<i>n</i> = 5)	20.7 (<i>n</i> = 3) > 30 (<i>n</i> = 4)

A, one patient > 30 minutes.

* 0.01 < *p* < 0.05
** *p* < 0.01 } compared with neostigmine 30 µg/kg.

T1/Tc of 95% was achieved within 10 minutes in all but two subjects, both of whom had received neostigmine 30 µg/kg. Recovery to a T4/T1 ratio of 0.75 took more than 10 minutes in three patients given neostigmine 30 µg/kg, three patients given neostigmine 60 µg/kg, and two patients given neostigmine 80 µg/kg. There was no statistical difference between the three reversal groups in speed of reversal to a T1/Tc of 95%, or a T4/T1 ratio of 0.75. However two patients in the neostigmine 30 µg/kg group failed to achieve a T4/T1 ratio of 0.75 within the 20-minute observation period, and thus total times to reach this ratio were not available in this group.

High dose neostigmine (80 µg/kg) achieved neither a T1/Tc of 95%, nor a TOF ratio of 0.75 faster than medium dose neostigmine (60 µg/kg) whatever the initial level of blockade. There was no decrease in the TOF ratio with the high dose neostigmine as might be expected if the antagonist contributed to, rather than reversed, the block.

Cardiovascular data (Fig. 3). Seventeen patients received low dose reversal (neostigmine 30 µg/kg) 16, medium dose (neostigmine 60 µg/kg) and 18, high dose (neostigmine 80 µg/kg). There was no difference among the groups in the resting heart rates or systolic blood pressures. The incidence of dysrhythmias was similar in all groups (Table 3). The blood pressures after reversal remained constant and within normal limits. The heart rates in all groups decreased gradually but significantly (*p* < 0.01) over the period of observation, but were generally within normal limits. Table 3 shows the number of patients in each group in whom the heart rate fell below 50 beats/minute.

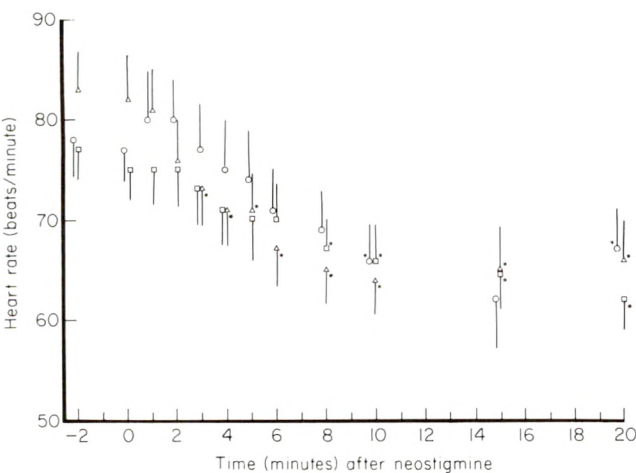


Fig. 3. Mean (SEM) heart rates after neostigmine. Δ , neostigmine 30 µg/kg; \square , neostigmine 60 µg/kg; \circ , neostigmine 80 µg/kg. * *p* < 0.01 compared with baseline (mean of -2 and 0 minute values).

Table 2. Moderate block. Recovery indices for 3 doses of neostigmine, mean (SEM).

	Dose of neostigmine, glycopyrronium. (µg/kg)		
	30/6 (low)	60/12 (medium)	80/16 (high)
<i>n</i>	6	6	7
% block of T1 at reversal	73.0 (1.6)	75.3 (1.4)	76.7 (0.7)
95% recovery of T1 (minutes)	10.5 (1.9)	6.8 (1.0)	6.6 (0.9)
T4/T1 = 0.75 (minutes)	8.2 (1.0)	10.0 (2.3)	8.0 (1.3)
(A)			
> 20 (<i>n</i> = 2)			

A, *n* = 4 for T4/T1 = 0.75 because 2 patients took > 20 minutes to achieve this.

Discussion

Neuromuscular data

Assessment of adequate reversal of neuromuscular blockade is a clinical decision. A T4/T1 ratio of 0.75 or greater has been suggested as an indicator of this⁸ and is taken as the yardstick in the study. Our data confirm that a prolonged time is necessary to reverse a very deep (> 90%) pancuronium-induced neuromuscular blockade. Neostigmine 80 µg/kg is higher than is normally recommended and proved no faster than the medium dose (60 µg/kg). There therefore appears to be no advantage to use more than neostigmine 60 µg/kg to reverse a profound block, and this dose may be optimum. None of the doses used, however, could be guaranteed to reverse the block in less than 30 minutes.

Complete reversal from a moderate block (approximately 75%) could not be achieved consistently with the low dose neostigmine (30 µg/kg) since two out of six patients took more than 20 minutes to reach a T4/T1 ratio of more than 0.75. The two higher doses of neostigmine reversed the block faster from this level, although in individual patients to achieve a T4/T1 ratio of 0.75 could also be prolonged. The high dose neostigmine (80 µg/kg) demonstrated no advantage over the moderate dose (60 µg/kg).

We saw no evidence of incomplete reversal or recurarisation with neostigmine 80 µg/kg, in spite of the theoretical possibility that too great a dose of neostigmine will increase fade and thus be less effective than a smaller dose.³ These results demonstrate that there should be a degree of spontaneous recovery before a reversal of a pancuronium-induced neuromuscular blockade. A train-of-four peripheral nerve stimulator can be used to ascertain this. Antagonism may take longer than 30 minutes no matter what the dose of reversal agent, if at the end of surgery the patient has a very deep (> 90%) block, which is indicated when only the first twitch of a TOF is present.⁹ In these circumstances the patient must be clinically assessed for the adequacy of reversal and ventilated if necessary until recovery. To antagonise a moderate (T1 70% to 80% of control) block, which corresponds to three twitches and the appearance of the fourth twitch of a TOF,⁹ a dose of neostigmine 30 µg/kg may still not be enough and 60 µg/kg will usually, but not always, provide reversal within 12 minutes. Therefore for antagonism of pancuronium in adults a dose of neostigmine in the order of 4–6 mg is usually appropriate, but even with this dose recovery may be prolonged if fewer than four twitches of a TOF are present.

Cardiovascular data

Glycopyrronium has been shown in several studies to have advantages over atropine in combination with neostigmine for antagonism of neuromuscular blockade.⁷ In contrast to atropine–neostigmine, the heart rate remains more stable after administration of glycopyrronium–neostigmine mix-

Table 3. Incidence of heart rate of 50 beats/minute or lower.

Neostigmine (µg/kg)	Time (minutes) to reversal												Number of Dysrhythmias*
	-2	0	1	2	3	4	5	6	8	10	15	20	
30 (<i>n</i> = 17)	0	0	0	1	1	1	1	2	2	2	2	4	5 (29%)
60 (<i>n</i> = 16)	0	0	0	0	0	2	2	1	1	0	2	3	8 (50%)
80 (<i>n</i> = 18)	0	0	0	0	0	0	0	0	0	1	1	1	4 (22%)

* all junctional except one first degree block.



tures,¹⁰ the incidence of dysrhythmias is lower,¹¹ the lack of central effects speeds arousal after general anaesthesia¹² and better control of secretions is produced.¹³ Bradycardia may occur if insufficient atropine is administered with large doses of neostigmine, because neostigmine has a dose-dependent duration of action.⁷ Glycopyrronium has a longer duration of action than atropine and might be superior in these circumstances. A ratio of neostigmine to glycopyrronium of 5:1 has been recommended since it causes least variation in heart rate.¹⁴ The response of heart rate after glycopyrronium has been shown to be dose related although it appears that the number of dysrhythmias is lowest with intermediate (10 µg/kg) doses compared with both higher and lower amounts.¹⁵

In this study neuromuscular blockade was antagonised towards the end of surgery and anaesthesia was continued for at least 20 minutes after reversal. The decrease in heart rate over time may be related to changes in surgical stimulation. The incidence of dysrhythmias was similar to that reported by others.¹⁶ All dysrhythmias resolved spontaneously and no untoward haemodynamic consequences occurred.

We realise that many factors may affect the cardiovascular effects of reversal agents. These include speed of injection,¹⁷ age of patient,¹⁸ anaesthetic agents,¹⁹ as well as the depth of anaesthesia and degree of surgical stimulation. Within these limitations our patients confirmed the cardiovascular suitability of a combination of neostigmine and glycopyrronium for reversal of neuromuscular blockade, and further demonstrated that a fixed ratio combination of 5:1 is acceptable over the range of clinically useful dosage.

Acknowledgments

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References

- MILLER RD, SAVARESE JJ. Pharmacology of muscle relaxants. In: MILLER RD ed. *Anesthesia*. New York: Churchill Livingstone, 1981: 518.
- FELDMAN SA. Competitive block—UK style. In: NORMAN J ed. *Clinics in Anaesthesiology Vol. 3*. Eastbourne: W.B. Saunders, 1985: 402.
- PAYNE JP, HUGHES R, AL AZAWI S. Neuromuscular blockade by neostigmine in anaesthetized man. *British Journal of Anaesthesia* 1980; **52**: 69–76.
- VIBY-MOGENSEN J, JENSEN NH, ENGBAERK J, ØRDRING H, SKOVGAARD LT, CHRAEMMER-JØRGENSEN B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology* 1985; **63**: 440–3.
- VIBY-MOGENSEN J, CHRAEMMER-JØRGENSEN B, ØRDRING H. Residual curarization in the recovery room. *Anesthesiology* 1979; **50**: 539–41.
- BEEMER GH, ROZENTAL P. Postoperative neuromuscular function. *Anaesthesia and Intensive Care* 1986; **14**: 41–5.
- MIRAKHUR RK, DUNDEE JW. Glycopyrrolate: pharmacology and clinical use. *Anaesthesia* 1983; **38**: 1195–1204.
- ALI HH, KITZ RJ. Evaluation of recovery from nondepolarizing neuromuscular block, using a digital neuromuscular transmission analyzer: preliminary report. *Anesthesia and Analgesia Current Researches* 1973; **52**: 740–4.
- VIBY-MOGENSEN J. Clinical assessment of neuromuscular transmission. *British Journal of Anaesthesia* 1982; **54**: 209–23.
- MIRAKHUR RK, DUNDEE JW. Glycopyrrolate-neostigmine mixture for antagonism of neuromuscular block: comparison with atropine-neostigmine mixture. *British Journal of Anaesthesia* 1977; **49**: 825–9.
- MOSTAFA SM, VUCEVIC M. Comparison of atropine and glycopyrronium in patients with pre-existing cardiac disease. *Anaesthesia* 1984; **39**: 1207–13.
- SHEREF SE. Pattern of CNS recovery following reversal of neuromuscular blockade. *British Journal of Anaesthesia* 1985; **57**: 188–191.
- COZANTIS DA, TUOMINEN M, KAUSTE A. The postoperative drying effects of atropine and glycopyrrolate. *Anaesthesia* 1982; **37**: 86–7.
- MIRAKHUR RK, DUNDEE JW, JONES CJ, COPPEL DL, CLARKE RSJ. Reversal of neuromuscular blockade: dose determination studies with atropine and glycopyrrolate given before or in a mixture with neostigmine. *Anesthesia and Analgesia* 1981; **60**: 557–62.
- MIRAKHUR RK, JONES CJ, DUNDEE JW. Effects of intravenous administration of glycopyrrolate and atropine in anaesthetised patients. *Anaesthesia* 1981; **36**: 277–81.
- HEINONEN J, SALMENPERÄ M, TAKKUNEN O. Advantages of glycopyrrolate over atropine during reversal of pancuronium block. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 147–50.
- HARPER KW, BALI IM, GIBSON FM, CARLISLE R, BLACK IHC, GRAINGER DJ, DUNDEE JW. Reversal of neuromuscular block. Heart rate changes with slow injection of neostigmine and atropine mixtures. *Anaesthesia* 1984; **39**: 772–5.
- MIRAKHUR RK. Antagonism of neuromuscular block in the elderly. *Anaesthesia* 1985; **40**: 254–8.
- SAMRA SK, PANDIT U, PANDIT SK, KOTHARY SP. Effect of halogenated anaesthetics on heart rate changes during reversal of neuromuscular block with glycopyrrolate and neostigmine. *Canadian Anaesthetists' Society Journal* 1984; **31**: 619–23.

The effect of changes in arm temperature on neuromuscular monitoring in the presence of atracurium blockade

E. A. THORNBERRY AND B. MAZUMDAR

Summary

This study was designed to investigate the relationship between arm temperature and the degree of blockade as monitored by peripheral nerve stimulation by a comparison of both arms of each patient; one exposed to the environment and the other wrapped to maintain its temperature. The decrease in the temperatures of the exposed arms were significantly more than the wrapped arms. A discrepancy was noted proportional to the temperature difference between the two arms, when the train-of-four counts were compared. A recommendation is made to maintain the temperature of the monitored arm above 32°C.

Key words

*Monitoring; neuromuscular blockade.
Neuromuscular relaxants; atracurium.*

The introduction of short acting muscle relaxants has led to the use of infusion techniques in which the rate of infusion is adjusted in accordance with the twitch response to a peripheral nerve stimulator. It is known that peripheral relaxation does not directly equal relaxation of the diaphragm.¹ It has been noted, however, that during prolonged anaesthesia monitoring becomes increasingly unreliable.^{2,3} Cooling of the arm used to monitor the patient has been postulated as the cause of this error.⁴ The aim of the study was to confirm this relationship and produce some guidelines for accurate monitoring.

Method

Consecutive patients with no contraindication to the use of atracurium who required a relaxant anaesthetic of greater than 2 hours duration were included in the trial. An oral or intramuscular premedication was prescribed as appropriate. Anaesthesia was induced with thiopentone 3–5 mg/kg, except for three patients who were given etomidate 0.3 mg/kg for increased cardiovascular stability. Atracurium 0.5 mg/kg was given to provide relaxation and anaesthesia was maintained with 66% nitrous oxide in oxygen supplemented with fentanyl and enflurane. An infusion of atracurium 0.5 mg/kg/hour was started 20 minutes after the initial dose of atracurium and the dose was adjusted to retain one twitch of a train-of-four stimulus. The infusion

was discontinued 10 minutes before the end of the operation and relaxation was reversed with neostigmine 2.5 mg and glycopyrronium 0.6 mg.

Right and left arm temperatures were monitored with peripheral skin temperature probes attached to the ventral aspect of each wrist. The arm with intravenous access was then exposed on an arm board while the other arm with the blood pressure cuff was wrapped in warm cotton wool and a towel in an attempt to maintain the original temperature. Core temperature was measured with an oesophageal temperature probe.

A train-of-four stimulus was applied to each arm from the same Bard peripheral nerve stimulator with two sets of leads and disposable skin electrodes. The patient was eliminated from the trial if a comparable response was not obtainable from each arm at the start of the operation, when the arm temperatures were the same. Readings of temperature and twitch response were recorded at 15-minute intervals. The theatre temperature was maintained between 21–25°C and warming blankets, blood warming coils and ventilator humidifiers were used to maintain body temperature.

Results

Twenty four patients were studied; four were eliminated because no comparable twitch responses were obtained at

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Dr Thornberry was awarded the President's medal for her presentation of part of this paper at the Junior Anaesthetists meeting in Belfast in April 1987.

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Table 1. Mean (SD) temperatures °C at the beginning and end of surgery.

	Mean core temperature °C	Mean temperature of exposed arm °C	Mean temperature of wrapped arm °C
Start	36.4 (0.59)	32 (1.24)	32 (1.46)
Finish	35.9 (1.02)	29.5 (2.46)	32 (1.03)

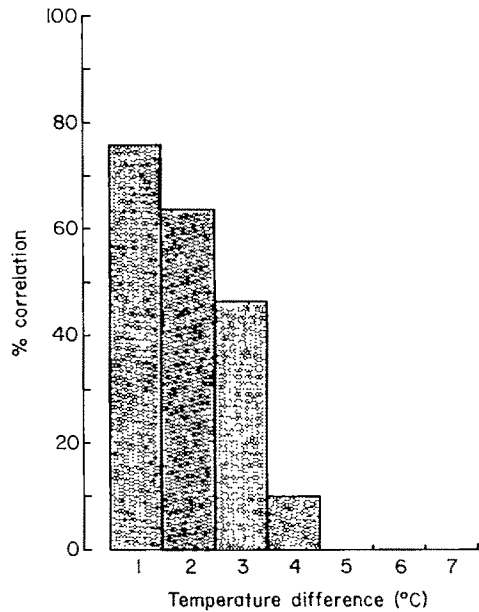


Fig. 1. The percentage correlation of twitch response in each arm related to the temperature difference between the two arms, in degrees Celsius.

the beginning of the studies. The mean age of the patients was 60 years (range 21–85; SD 15.75) and the mean duration of the operations was 3.7 hours (range 2–8 SD 1.52).

The temperatures recorded are shown in Table 1. The temperature differences between the two arms at the end of the operations were statistically significant ($p < 0.001$ Wilcoxon Rank Sum Test). The train-of-four counts were compared; if they were the same they were recorded as correlating, but if the number of twitches differed they were recorded as not correlating. The results were grouped according to the temperature difference between each arm. The percentage correlation compared with the temperature difference (°C) is shown in Fig. 1. A comparison of the percentage correlation compared with the temperature of the cool arm is shown in Fig. 2.

Discussion

The results show a significant difference between the temperatures of the exposed and wrapped arms at the end of the operations and the correlation of the train-of-four responses decreased as the temperature difference increased. Only when both arm temperatures were above 32°C was there 100% correlation between the two arms. The possible causes of the apparent selective depression of neuromuscular conduction in the cool arms of our patients are threefold. Firstly, the direct effects of temperature on the nerve and muscle, secondly, a localised block by atracurium, and thirdly, interference with the monitoring by changes in skin impedance. The effects of temperature on muscle and nerve have been described in detail by Feldman.⁵ He suggested

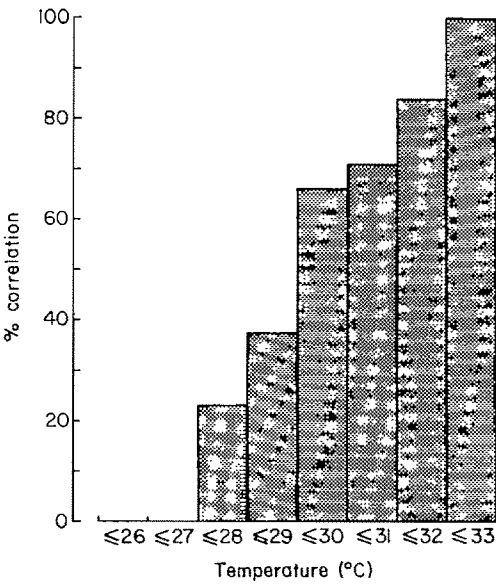


Fig. 2. The percentage correlation of twitch response in each arm related to the temperature of the cooler arm, in degrees Celsius.

the causes of reduced neuromuscular conduction are a combination of delayed nerve conduction time; delayed repolarisation of the nerve spike potential; a slow rate of release of acetylcholine; a reduced rate of generation of muscle contraction and decreased muscle tension. The most significant of these appears to be the slow rate of release of acetylcholine⁶ which explains why the reduced twitch height with cooling is reversible with edrophonium or tetanic stimulation. Feldman studied five patients who had surgery under profound hypothermia without muscle relaxants and showed a steady decline in twitch heights recorded in the arm as the temperature dropped below 34°C. Thornton, Blakeney and Feldman demonstrated, in dogs, complete block in conduction between nerve and muscle at 28°C in the cooled limb.⁶

Unlike curare, atracurium is not antagonised by hypothermia.⁷ Instead the duration of action has been shown to be prolonged. This was originally thought to be because it is broken down by Hofmann degradation which is dependant upon temperature and hydrogen ion concentration. However, a recent study by Denny and Kneeshaw which compared the behaviour of atracurium with vecuronium under hypothermia showed no difference between these two drugs⁸ which suggests the Hofmann elimination is not responsible. This is supported by recent evidence that ester hydrolysis is the major metabolic pathway of atracurium.⁹ Denny and Kneeshaw concluded that the reduced rate of release of acetylcholine caused slower dissociation of the relaxant from the motor end plate.⁸ Suggestions have been made that temperature-related changes in skin impedance may interfere with peripheral nerve monitoring when skin

electrodes are used,¹⁰ which give a false impression of paralysis. The Bard peripheral nerve stimulator is a fixed voltage stimulator so that the current which reaches the arm is proportional to the impedance. A digital read out of the actual current which reaches the patient is continuously displayed. No difference was noted in the current to each arm throughout each case which suggested there was no significant increase in impedance. This could be because of the good electrical contact obtained with the pre-jelled skin electrodes.

Conclusion

The use of some form of peripheral nerve stimulator to monitor neuromuscular blockade is rapidly becoming routine especially with the increased use of infusions of relaxants. Many hospitals rely on simple peripheral nerve stimulators with a train-of-four stimulus for this purpose and count the number of twitches in response. Frequent references have been made in the literature to the need to maintain the arm temperature^{2,4,10} which can be achieved by wrapping the arm in warm cotton wool and a towel. The conclusion of this study is that to ensure more accurate neuromuscular monitoring every effort must be made to maintain arm temperature above 32°C.

Acknowledgments

We are grateful to Dr J. Moon and Mr G. Prout for allowing us to study their patients, and to Dr D. Saunders for his invaluable advice and encouragement both with the

statistics and the preparation of this paper. We also thank the department of Teaching Media for their help in preparing the histograms.

References

1. CHAUVIN M, LEBRAULT C, DUVALDESTIN P. The neuromuscular blocking effect of vecuronium on the human diaphragm. *Anesthesia and Analgesia* 1987; **66**: 117-22.
2. JONES RM. Neuromuscular transmission and its blockade. *Anaesthesia* 1985; **40**: 964-76.
3. ASTLEY BA, HACKETT H, HUGHES R, PAYNE JP. Recovery of respiration following neuromuscular blockade with atracurium and alcuronium. *British Journal of Anaesthesia* 1986; **58**: 75S-79S.
4. DENNY NM, BETHUNE DW, HARDY I, KNEESHAW JD, LATIMER RD. Apparent postoperative recurarisation. *Anaesthesia* 1986; **41**: 440-1.
5. FELDMAN SA. *Muscle relaxants*. Philadelphia: W.B. Saunders, 1973: 117-22.
6. THORNTON RL, BLAKENEY C, FELDMAN SA. The effect of hypothermia on neuromuscular conduction. *British Journal of Anaesthesia* 1976; **48**: 264.
7. FLYNN PJ, HUGHES R, WALTON B. Use of atracurium in cardiac surgery involving cardiopulmonary bypass with induced hypothermia. *British Journal of Anaesthesia* 1984; **56**: 967-72.
8. DENNY NM, KNEESHAW JD. Vecuronium and atracurium infusions during hypothermic cardiopulmonary bypass. *Anaesthesia* 1986; **41**: 919-22.
9. STILLER RL, RYAN COOK D, CHAKRAVORTI S. *In vitro* degradation of atracurium in human plasma. *British Journal of Anaesthesia* 1985; **57**: 1085-8.
10. FOX MA, HUNTER JM. Apparent postoperative recurarisation. *Anaesthesia* 1986; **41**: 879-80.

Recovery of neuromuscular function and postoperative morbidity following blockade by atracurium, alcuronium and vecuronium

K. L. KONG AND G. M. COOPER

Summary

Recovery of neuromuscular function and postoperative morbidity were studied in 51 fit female patients who had nonemergency gynaecological laparoscopy as inpatients. They were allocated randomly to one of three groups to receive either atracurium 0.31 mg/kg, alcuronium 0.25 mg/kg, or vecuronium 0.06 mg/kg as part of an otherwise standard anaesthetic technique. There were neither differences in intubation conditions nor in the occurrence of postoperative diplopia whichever muscle relaxant was used. Deficits in grip strength and expiratory force were seen at one hour after reversal with atropine 1.2 mg and neostigmine 2.5 mg in all patients, deficits which persisted for 3 hours in those who received alcuronium. The recovery of inspiratory force was slower and less complete at up to 3 hours in those who received alcuronium and there was a high incidence of minor postoperative morbidity at up to 24 hours in each of the three groups. The only statistical difference in symptomatic morbidity was an increase in muscle weakness in those who received alcuronium compared with atracurium at 3 hours after laparoscopy. Only 25%, 20% and 31% of the patients who received atracurium, alcuronium and vecuronium respectively said that they would have liked to be day stay patients.

Key words

*Muscle relaxants; alcuronium, atracurium, vecuronium.
Surgery; day stay, gynaecological.*

The majority of anaesthetists (96%)¹ consider that tracheal intubation is indicated for laparoscopy because of the need to protect the airway from gastric aspiration and to assist or control ventilation. Tracheal intubation is achieved most safely with muscle relaxants, the choice of which is normally decided by a balance of the speed of onset required, the duration of action, side effects and the cost of the drug.

Laparoscopy is usually a short procedure and in the absence of complications some patients are treated as day cases. In the hospital where we work, however, patients scheduled for gynaecological laparoscopy are currently treated as inpatients. The newer, shorter-acting muscle relaxants, atracurium and vecuronium, have been shown to be suitable for daycase laparoscopy.² However, some of our anaesthetic colleagues are sceptical about whether there is any discernible clinical benefit in the use of atracurium or vecuronium in preference to alcuronium for laparoscopy. Unable to find a comparison, we have studied the recovery of neuromuscular function following blockade with equipotent doses^{3,4} of atracurium, alcuronium or vecuronium for gynaecological laparoscopy to see whether any differences are clinically important and

whether they contribute to the ability to go home on the day of surgery.

Methods

Fifty-one female patients (ASA 1) scheduled for gynaecological laparoscopy and who gave informed consent were studied, after hospital ethical committee approval had been obtained. Patients were allocated randomly to receive either atracurium 0.31 mg/kg (group I), alcuronium 0.25 mg/kg (group II), or vecuronium 0.06 mg/kg (group III) as part of the anaesthetic technique. All patients were premedicated with oral temazepam 20 mg one hour before surgery and anaesthesia was induced with a sleep dose of thiopentone. The patients' lungs were ventilated with 1% halothane in 67% nitrous oxide in oxygen for 3 minutes after the muscle relaxant had been given; the trachea was then intubated by one of the authors who was unaware of which muscle relaxant had been administered. Intubation conditions were graded according to the criteria of Gergis and colleagues⁵ as excellent, good, poor or impossible, and anaesthesia was maintained by ventilation to normocapnia with 0.5% halothane in 67% nitrous oxide in oxygen. The electro-

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cardiogram was monitored continuously and pulse rate and arterial blood pressure were recorded every 5 minutes. The bladder was catheterised, after the patient was placed in the Lloyd Davis supports, and laparoscopy was performed routinely with carbon dioxide as the insufflating gas and with patient tilted head-down. Care was taken to expel as much carbon dioxide gas as possible before removal of the trocar at the end of the procedure, when neuromuscular blockade was antagonised with neostigmine 2.5 mg and atropine 1.2 mg.

Before premedication and at one, 2 and 3 hours post-operatively each patient completed tests of muscle power;⁶ grip strength was measured to the nearest 50 mmHg on compression of 30 ml of air in a 60-ml syringe using a Class I Bourdon type sensor brass gauge. The maximum inspiratory force when inhaling from residual lung volume and the maximum expiratory force when exhaling from maximum lung volume were recorded to the nearest 2.5 mmHg on a Class I Capsule-type sensor brass gauge. The patients were instructed in the use of the equipment before premedication and once familiarised the mean of three readings for each test was recorded pre-operatively and at the postoperative assessments. The presence or absence of diplopia when a patient looked at a single line ahead and to the sides was also noted. Neither the patient nor the observer was aware of which muscle relaxant had been administered.

Patients were questioned about the presence or absence of muscle weakness, muscle pain, dizziness, nausea, vomiting, abdominal pain, shoulder pain, headache and sore throat at the end of the third hour after laparoscopy. The same questions were asked on a questionnaire the following day before discharge from hospital and also whether the patient would have liked to go home on the same day as her laparoscopy.

Results were analysed using the Chi-square test (with Yates' correction for small numbers) for intubation conditions, occurrence of postoperative diplopia and post-operative morbidity. Grip strength, inspiratory force and expiratory force were analysed by paired Student's *t*-test within groups and by unpaired Student's *t*-test between groups.

Results

In each group there were 17 patients who were comparable in age, weight and duration of laparoscopy (Table 1). Seven patients in group I and six each from groups II and III had diagnostic laparoscopy while the remainder had double portal entry, clip sterilisation. There were no differences between intubation conditions in the groups (Table 2) and in all but one patient they were graded as good or excellent. Postoperative diplopia was present in six patients from group I, eight patients from group II and four patients from group III. These differences were not significant. In all three groups assessment of recovery from neuromuscular blockade (Tables 3, 4 and 5) showed comparable pre-operative baseline values and a deficit in grip strength one hour after laparoscopy ($p < 0.01$). In group II this deficit persisted for 3 hours ($p < 0.001$) while in group III it was still seen at 2 hours but not at 3 hours. No deficit was seen in group I at either 2 or 3 hours. The deficit in group II at one hour and at 2 hours

Table 1. Patient data. Values expressed as mean (range).

	Group I, atracurium (n = 17)	Group II, alcuronium (n = 17)	Group III, vecuronium (n = 17)
Age, years	33.9 (19-52)	32.3 (23-44)	34.1 (23-47)
Weight, kg	60.9 (50-78)	64.4 (53-82)	62.8 (50-86)
Duration of laparoscopy, minutes	23.5 (18-33)	23.0 (18-31)	25.5 (19-32)

Table 2. Assessment of the conditions for intubation.

	Group I, atracurium (n = 17)	Group II, alcuronium (n = 17)	Group III, vecuronium (n = 17)
Excellent	10	14	13
Good	6	3	4
Poor	1	0	0

was also greater ($p < 0.01$ and $p < 0.05$ respectively) than that in groups I and III.

Group II showed decreased inspiratory force at one, 2 and 3 hours whereas inspiratory force was reduced in group III at one hour only; no deficit was seen in group I. Groups I, II and III showed reduced expiratory force at one hour ($p < 0.01$), a deficit which persisted for 3 hours in group II ($p < 0.01$) and for 2 hours in group III. In group I no deficit was seen at 2 and 3 hours. Group II showed a decreased expiratory force when compared with group I at one and 2 hours ($p < 0.01$) and at 3 hours ($p < 0.05$). Results of the questionnaire for three patients at 3 hours and four patients at 24 hours were unavailable. The only statistically significant difference between the three groups with regard to postoperative morbidity at 3 hours was an increased incidence of muscle weakness in those who received alcuronium compared with those who received atracurium. Most patients mentioned abdominal pain as a problem (Tables 6 and 7) and 15 patients from group I, 12 patients from group II and 11 patients from group III received postoperative analgesia. Twenty five, 20 and 31 percent of the patients who received atracurium, alcuronium and vecuronium respectively said that they would have liked to be day stay patients.

Discussion

Like the majority of anaesthetists we prefer to intubate patients who have laparoscopy. The choice and dose of muscle relaxant for what is usually a very short procedure is a balance between how to obtain satisfactory conditions for intubation and achieve adequate reversal some 20 to 30 minutes later. Use of suxamethonium can overcome this but at the expense of increased incidence and severity of muscle, neck and shoulder pains^{7,8} which is undesirable, especially for day cases. We preferred to use a non-depolarising agent and chose the dose of alcuronium which it was our practice to use for laparoscopy. We knew that it provided satisfactory conditions for intubation and that patients breathed satisfactorily at the end of the procedure. We were unable to find a single study which gave data for equipotent dosages of atracurium and vecuronium in relation to alcuronium. Two studies^{3,4} found very similar ED95 doses (62.2 and 64.4 ug/kg) for pancuronium and from these the potency ratios for atracurium, alcuronium and vecuronium at ED95 were calculated for our study. A

Table 3. Grip strength in mmHg. Values are expressed as mean (SD).

	Group I, atracurium (<i>n</i> = 17)		Group II, alcuronium (<i>n</i> = 17)		Group III, vecuronium (<i>n</i> = 17)
Baseline	985 (130)		1032 (122)		1012 (99)
1 hour	799 (191)**	-- + + --	547 (232)**	-- + + --	841 (166)**
2 hours	901 (155)	-- + --	762 (215)**	-- + --	912 (150)**
3 hours	918 (159)		796 (232)	-- + --	962 (133)

** Significant differences from baseline ($p < 0.01$).+ Significant differences between groups ($p < 0.05$).+ + Significant differences between groups ($p < 0.01$).**Table 4.** Inspiratory force in mmHg. Values are expressed as mean (SD).

	Group I, atracurium (<i>n</i> = 17)		Group II, alcuronium (<i>n</i> = 17)		Group III, vecuronium (<i>n</i> = 17)
Baseline	44 (11)		44 (11)		40 (14)
1 hour	35 (15)	-- + --	25 (13)**		28 (16)*
2 hours	41 (15)		32 (13)**		35 (16)
3 hours	45 (14)	-- + --	35 (13)*		44 (17)

* Significant differences from baseline ($p < 0.05$).** Significant differences from baseline ($p < 0.01$).+ Significant differences between groups ($p < 0.05$).**Table 5.** Expiratory force in mmHg. Values expressed as mean (SD).

	Group I, atracurium (<i>n</i> = 17)		Group II, alcuronium (<i>n</i> = 17)		Group III, vecuronium (<i>n</i> = 17)
Baseline	42 (9)		43 (10)		41 (10)
1 hour	30 (9)**	-- + + --	17 (8)**	-- + --	25 (14)**
2 hours	36 (9)	-- + + --	24 (7)**		29 (13)**
3 hours	40 (11)	-- + --	30 (11)**		36 (12)

** Significant differences from baseline ($p < 0.01$).+ Significant differences between groups ($p < 0.05$).+ + Significant differences between groups ($p < 0.01$).**Table 6.** Postoperative morbidity at 3 hours.

	Group I, atracurium (<i>n</i> = 16)		Group II, alcuronium (<i>n</i> = 15)		Group III, vecuronium (<i>n</i> = 17)
Muscle weakness	4	---*---	10		6
Muscle pain	2		1		0
Dizziness	4		5		5
Double vision	6		7		3
Nausea	5		9		7
Vomiting	1		3		4
Abdominal pain	16		15		16
Shoulder pain	3		3		3
Headache	1		4		3
Sore throat	2		5		7

* Significant difference ($p < 0.05$).

discrepancy was found, however, in their ED95 dose of vecuronium (56.2 and 36.1 $\mu\text{g/kg}$) in relation to pancuronium. We chose the smaller dose of vecuronium and this provided as good conditions for intubation as seen with both alcuronium and atracurium (see Table 2). It seemed reasonable to extrapolate the larger than ED95 doses as the log/dose response curves were parallel and straight.

Neuromuscular block appeared, by clinical assessment, to be well reversed in all patients who breathed satisfactorily after neostigmine and atropine administration. We considered use of a peripheral nerve stimulator, in a pilot study, but found that we would not have been 'blind' to which muscle relaxant had been administered. We considered this to be important in the assessment of the

indices of postoperative neuromuscular function: we might have affected the patients' performance and encouraged them to perform optimally at the tests of grip strength, and inspiratory and expiratory effort.

We were able to demonstrate clearly a more rapid recovery from atracurium and vecuronium than from alcuronium with the tests of neuromuscular recovery which we used. This is interesting as Fragen and Shanks who compared vecuronium and pancuronium for laparoscopy unsurprisingly found no measurable difference between the agents only 30 minutes after surgery. In our study, with regard to grip strength, inspiratory and expiratory forces, those who received alcuronium were still significantly impaired compared with their baseline values 3 hours after laparoscopy.

Table 7. Postoperative morbidity from 3 to 24 hours.

	Group I, atracurium (n = 16)	Group II, alcuronium (n = 15)	Group III, vecuronium (n = 16)
Muscle weakness	6	5	5
Muscle pain	6	4	3
Dizziness	7	6	2
Double vision	1	3	0
Nausea	6	6	4
Vomiting	2	5	3
Abdominal pain	11	11	10
Shoulder pain	8	7	10
Headache	6	7	4
Sore throat	8	6	12
Would like day stay	4	3	5

Patients in pain may be unlikely to perform the tests, especially those related to breathing, as well as those who are comfortable. Analgesia (intramuscular papaveretum) was given as requested and similar numbers of patients in each group required it. Hence, any differences between the groups were unlikely to be due to pain or the provision of analgesia.

The symptoms recorded on the questionnaire which we felt might be attributed to the muscle relaxant were muscle weakness and double vision. Those who received alcuronium complained more of subjective muscle weakness than those who received atracurium at 3 hours after laparoscopy but no differences were seen in the incidence of double vision. A study¹⁰ which compared atracurium and alcuronium for laparoscopy found an increased incidence of minor morbidity 24 hours later in those patients who received alcuronium. The authors postulated that this was due to a longer neuromuscular block which caused incoordination and muscular strain for a varied length of time. It is possible that the period of bedrest in our group of inpatients was sufficient to prevent an increase in minor morbidity 24 hours later in those who received alcuronium.

Like other workers^{2,8,10-12} we found a high incidence of minor postoperative morbidity and these symptoms often distressed patients enough to prevent them from wanting to go home the same day. However, all patients felt sufficiently well to go home on the morning after laparoscopy. Overall only 26% of our inpatients would have liked to be day stay patients compared with two other studies on outpatients^{10,13} where 30% would have preferred to stay in hospital overnight. These findings emphasise the need for careful patient selection for day-case laparoscopy. We have shown that atracurium and

vecuronium have significant advantages for recovery of muscle power which make these agents especially attractive for use where daycase laparoscopy is indicated.

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References

1. CHAMBERLAIN G, CARRON-BROWN, JA. Gynaecological laparoscopy. *Report of the working party of the confidential enquiry into gynaecological laparoscopy* 1978; Royal College of Obstetricians and Gynaecologists.
2. SENGUPTA P, SKACEL M, PLANTEVIN OM. Postoperative morbidity associated with the use of atracurium and vecuronium in day-case laparoscopy. *European Journal of Anaesthesiology* 1987; 4: 93-9.
3. GRAMSTAD L, LILLEAASEN P. Dose-response relation for atracurium, Org NC45 and pancuronium. *British Journal of Anaesthesia* 1982; 54: 647-51.
4. KREIG N, CRUL JF, BOOU LHDJ. Relative potency of OrgNC 45, pancuronium, alcuronium and tubocurarine in anaesthetised man. *British Journal of Anaesthesia* 1980; 52: 783-8.
5. GERGIS SD, SOKOLL MD, METHTA M, KEMMOTSU O, RUDD GD. Intubation conditions after atracurium and suxamethonium. *British Journal of Anaesthesia* 1983; 55: 835-86S.
6. BURCHETT K, MADDEN AP, HUTTON P. A comparison of neuromuscular recovery following blockade by atracurium and pancuronium. *British Journal of Anaesthesia* 1985; 57: 338P.
7. DHAMEE MS, GANDHI SK, CALLEN KM, KALBFLEISH JH. Morbidity after outpatient anaesthesia—a comparison of different endotracheal anesthetic techniques for laparoscopy. *Anesthesiology* 1982; 57: A375.
8. SKACEL M, SENGUPTA P, PLANTEVIN OM. Morbidity after day case laparoscopy. A comparison of two techniques of tracheal anaesthesia. *Anaesthesia* 1986; 41: 537-41.
9. FRAGEN J, SHANKS CA. Neuromuscular recovery after laparoscopy. *Anesthesia and Analgesia* 1984; 63: 51-4.
10. COLLINS KM, PLANTEVIN OM, DOCHERTY PW. Comparison of atracurium and alcuronium in day-case gynaecological surgery. *Anaesthesia* 1984; 39: 1130-4.
11. TRACEY JA, HOLLAND AJC, UNGER L. Morbidity in minor gynaecological surgery: a comparison of halothane, enflurane and isoflurane. *British Journal of Anaesthesia* 1982; 54: 1213-5.
12. KENEFICK JP, LEADER A, MALTBY JR, TAYLOR PJ. Laparoscopy: blood-gas values and minor sequelae associated with three techniques based on isoflurane. *British Journal of Anaesthesia* 1987; 59: 189-94.
13. KURER FL, WELCH DB. Gynaecological Laparoscopy: clinical experiences of two anaesthetic techniques. *British Journal of Anaesthesia* 1984; 56: 1207-12.

A comparison of isoflurane and halothane in anaesthesia for intra-ocular surgery

J. F. CRAIG AND J. H. COOK

Summary

Isoflurane 0.75% was compared with halothane 0.5% as the volatile supplement in a normocapnic technique for intra-ocular surgery. Both agents gave satisfactory conditions for operation with a comparable reduction in intra-ocular pressure during the procedure. Systolic arterial pressure, however, was significantly lower in the isoflurane group at the end of surgery and after tracheal extubation than in the halothane group. Isoflurane provides a useful alternative to halothane in anaesthesia for intra-ocular surgery.

Key words

Anaesthetics, volatile; halothane, isoflurane.

Measurement techniques; intra-ocular pressure.

The advantages of an anaesthetic technique for intra-ocular surgery which incorporates normocapnic ventilation supplemented with a volatile agent have been described previously.¹ Halothane, enflurane^{2,3} and to a lesser extent trichloroethylene⁴ used in this way produce a satisfactory reduction in intra-ocular pressure (IOP), whilst normocapnia maintains cardiac output⁵ and facilitates a rapid return to spontaneous ventilation at the end of the procedure.

Isoflurane, the newest and least soluble volatile anaesthetic agent,⁶ provides a more favourable cardiac index than halothane or enflurane⁷ which in the predominantly elderly population who present for cataract extraction may be an advantage. The purpose of this study was to compare approximately equipotent doses of isoflurane and halothane in a technique which incorporates normocapnic ventilation with special reference to IOP and arterial pressure.

Methods

Permission to carry out the study was obtained from the local ethical committee. Thirty patients admitted for routine cataract surgery under the care of one ophthalmic surgeon were allocated randomly by the sealed envelope technique to an isoflurane or halothane group. Patients gave informed consent at the pre-operative visit and were weighed. There was no attempt to select patients but those who had had previous cataract extraction on the eye to be studied were excluded. Atropine 0.6 mg was administered

intramuscularly as premedication between 60 and 90 minutes before anaesthesia.

Patients were moved directly on to the operating table, on arrival in the operating theatre suite, where monitoring with an electrocardiograph (Cardiorater) and an automatic blood pressure recorder (Dinamap model 845) was established. Amethocaine 1% drops and fluorescein from a dye-impregnated paper strip were instilled into the conjunctival sac of the eye not scheduled for surgery, and control measurements were made of pulse, arterial blood pressure and IOP, the latter using a Perkins' hand-held applanation tonometer.⁸ Measurements of IOP were all made by one person (J.H.C.) with patients supine in the position for surgery.

Anaesthesia was induced via an indwelling 23-gauge intravenous needle (Abbott Butterfly) in the dorsum of the left hand, with thiopentone 4 mg/kg followed by atracurium 0.6 mg/kg, each drug flushed through the needle with 1 ml 0.9% saline. The lungs were then mechanically inflated with 33% oxygen in nitrous oxide via a face mask with the Penlon version of the Bain anaesthetic breathing system⁹ driven by a Nuffield 200 series ventilator (Penlon Ltd).

The ventilator controls were adjusted in order to maintain normocapnia.^{10,11} The inspiratory and expiratory times of the ventilator were set at 1.5 and 3.5 seconds respectively, to give a respiratory rate of 12 breaths/minute, and the inspiratory rate control adjusted so that the tidal volume delivered was 10 ml/kg measured by a Wright's respirometer at the patient end of the system. The flow-

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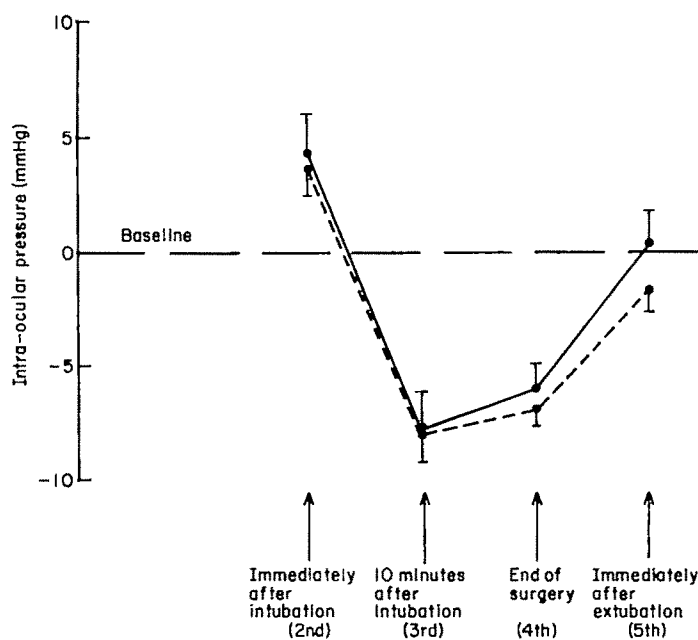


Fig. 1. Intra-ocular pressure changes in mmHg during and after general anaesthesia with halothane (—) and isoflurane (---) (mean, SEM; $n = 15$).

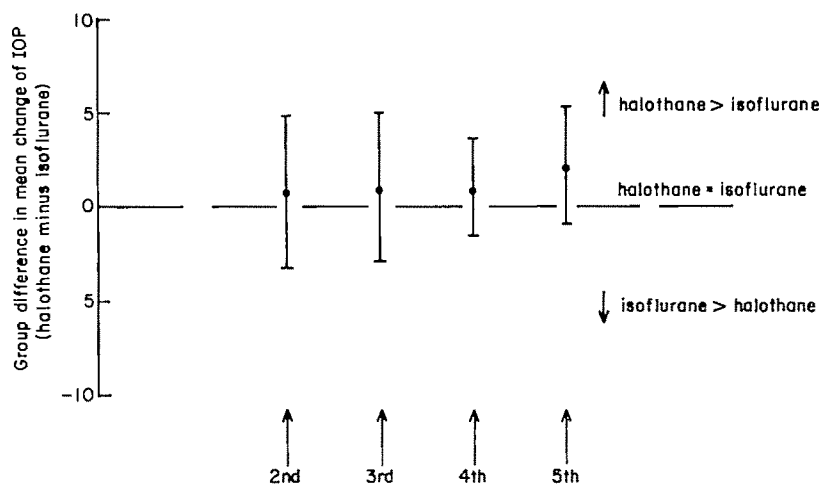


Fig. 2. Differences, and 95% confidence intervals, between the two groups in mean change of intra-ocular pressure in mmHg during and after general anaesthesia with halothane and isoflurane.

Table 1. Patient characteristics (median age with range; mean weight (SEM) with range).

	Isoflurane	Halothane
Number of patients	15	15
Males:females	6:9	5:10
Age, years/range	75 61–85	79 48–90
Weight, kg(SEM)range	65.6 (2.9) 40–87	64.1 (3.3) 43–88

meters were set to yield a fresh gas flow as near as possible to 70 ml/kg/minute. This was supplemented with 0.75% isoflurane from a Fortec vaporizer (Cyprane Ltd) or 0.5% halothane from a Fluotec Mark III vaporizer (Cyprane Ltd), depending on the group allocation of the patient. Both vaporizers had been checked for correct calibration with the Normac anaesthetic monitor (Vickers Medical).

Tracheal intubation was performed 3 minutes after induction of anaesthesia, with a cuffed tracheal tube, after the larynx and trachea had been sprayed with 4% lignocaine 4 ml, and ventilation continued as before. Once the tidal volume had been checked again the Wright's respirometer was removed from the system. Pulse, systolic arterial pressure and IOP were measured immediately after tracheal intubation and again 10 minutes later. Surgery then started.

Neuromuscular blockade was assessed with a peripheral nerve stimulator attached via two small ECG electrodes over the left ulnar nerve in the forearm and palpating the twitch response to train-of-four supramaximal stimuli every 5 minutes. When the fourth stimulus produced a palpable flexion a supplement of atracurium 5 mg was given intravenously. Pulse, systolic arterial

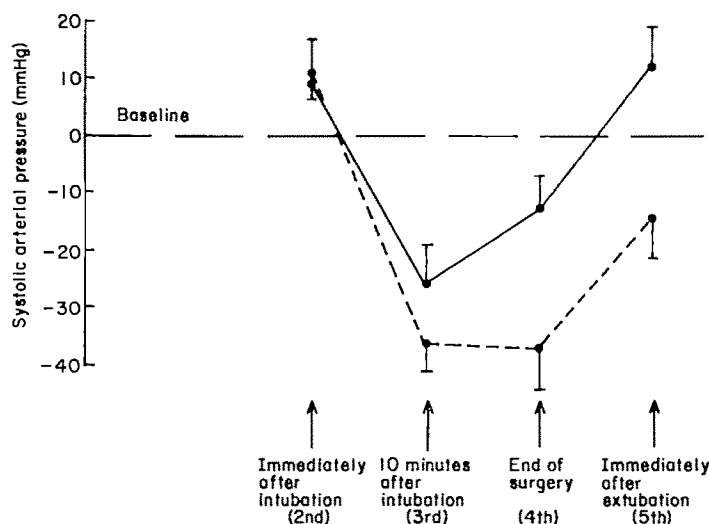


Fig. 3. Changes in systolic arterial pressure in mmHg during and after general anaesthesia with halothane (—) and isoflurane (---) (mean, SEM; $n = 15$).

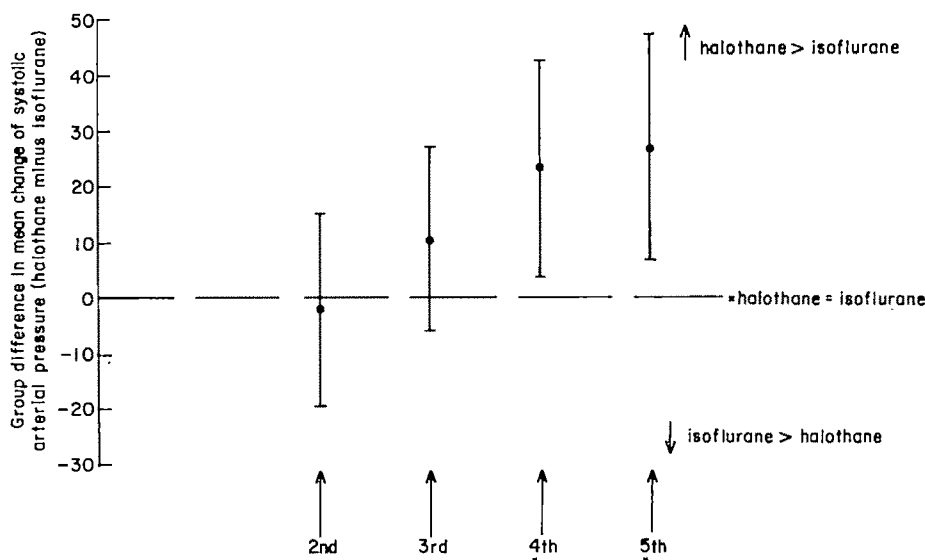


Fig. 4. Differences, and 95% confidence intervals, between the two groups in mean change of systolic arterial pressure during and after general anaesthesia with halothane and isoflurane (* $p < 0.05$).

pressure and IOP were measured and neuromuscular blockade antagonised with neostigmine 2.5 mg and atropine 0.6 mg, at the end of the procedure. Complete reversal of paralysis was indicated by return of four equal twitches in response to a train-of-four stimulation. The vaporizer was turned off and the lungs ventilated with 100% oxygen with the same ventilatory parameters, and the pharynx cleared of secretions. The final measurements of pulse, systolic blood pressure and IOP were made after tracheal extubation and the patient returned to the recovery area breathing oxygen-enriched air through a plastic disposable facemask until consciousness returned.

Statistical analysis was performed using the Student's t -test for quantitative data. Ninety-five percent confidence limits were derived for all data. The critical level of significance was $p < 0.05$.

Results

The 15 patients in each group were well matched for age and weight (Table 1).

There were small differences between the two groups at the pre-induction time in both IOP and systolic arterial pressure. Student's t -test indicated that these differences were not significant but allowance was made by comparing changes from the control value in each group. Figure 1 shows the changes in mean IOP from the control value in the two groups. Both groups of patients showed an increase in IOP in response to intubation followed by a decrease to below control value 10 minutes after intubation. IOP was maintained in both groups at this lower value throughout the procedure but after withdrawal of anaesthesia and reversal of neuromuscular blockade IOP tended to return to pre-induction values. There was no statistically significant

difference between the two groups at any of the times of measurement. This is further qualified by the 95% confidence limits shown in Fig. 2. Figure 3 shows the changes in mean systolic arterial pressure from control in the two groups. There was a pressor response to intubation in both groups followed by a moderate fall after 10 minutes to below control values. This reduction was maintained in the isoflurane group throughout the procedure but in the halothane group there was a tendency for values to return towards control by the end of surgery. The difference between the groups at this point (the fourth measurement) was significant, $p < 0.05$. The systolic arterial pressure after extubation had risen to a level above the control in the halothane group, but remained below control in the isoflurane group. This difference was also significant, $p < 0.05$. The 95% confidence limits shown in Fig. 4 demonstrate the significance of these values; the readings at the fourth and fifth measurements all lie above the line of no difference.

Discussion

The two agents compared in this study were used in compatible concentrations according to their MAC values in 70% nitrous oxide (0.5% for isoflurane and 0.29% for halothane).⁶ Normocapnia was maintained with the Bain system with a fresh gas flow of 70 ml/kg in a standard anaesthetic technique, which had been used to assess the effect of other drugs on intra-ocular pressure.^{1,3}

Atracurium was the muscle relaxant chosen for its advantages of rapid and complete recovery from blockade together with relative cardiovascular stability.^{12,13} It was felt necessary to monitor the level of neuromuscular blockade to avoid the possibility of voluntary movement because spontaneous offset of block is relatively rapid with this agent.

Halothane 0.5% and enflurane 1% (MAC equivalents) have been compared in previous studies. In one of these, a greater reduction in IOP was found intra-operatively in an enflurane group (40%) than in a halothane group (14%), whilst other authors have demonstrated a 50% reduction in IOP with halothane and a 35% reduction with enflurane.³ The latter agent however, is associated with a greater intra-operative fall in systolic arterial pressure. Trichloroethylene 0.4% used in a similar technique⁴ was shown to lower IOP 10 minutes after induction, but thereafter the IOP tended to increase despite a constant systolic and mean blood pressure which indicated that trichloroethylene caused a dose-related rise in IOP.

Isoflurane has gained in popularity since its introduction into clinical practice and its advantages in terms of cardiovascular stability, solubility and resistance to metabolism, have been well documented.⁷ Its effect on IOP during controlled ventilation of the lungs, however, has not been studied previously, although isoflurane was found to reduce IOP in children who were unsedated prior to induction.¹⁴

A satisfactory perioperative reduction in IOP occurred in both the halothane and isoflurane groups but neither agent was able to obtund the pressor response¹⁶ to intubation. The lower systolic arterial pressure in the isoflurane group at the end of surgery and after extubation was predictable from the known effects of isoflurane on peripheral vascular resistance^{6,16} but this was not a problem clinically; the

lowest recorded systolic arterial pressure was 97 mmHg in two cases in the isoflurane group. The incidence of cardiac dysrhythmias was not specifically compared but no patient in either group required treatment for disturbance of cardiac rhythm.

Intra-ocular pressure is maintained in the normal eye at 16 (SD 5) mmHg by a balance between the volume of aqueous humour, vitreous and choroid vasculature which exert an outward pressure from within the globe, and scleral compliance and extra-ocular muscle tone which press inwards.¹⁷ Volatile agents such as halothane and isoflurane may reduce IOP indirectly through their effect on the cardiovascular system,³ despite autoregulation of choroidal blood flow, but may also facilitate drainage of aqueous¹⁸ by the direct muscle relaxant effect on extra-ocular muscles and the orbicularis oculi.

In conclusion, isoflurane used in this technique gives satisfactory conditions for intra-ocular surgery and if indicated on grounds of cardiac stability or to avoid repeat exposure to halothane would provide a useful alternative agent.

Acknowledgments

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References

- ADAMS AP, FREEMAN A, HENVILLE JD. Normocapnic anaesthesia for intra-ocular surgery. *British Journal of Ophthalmology* 1979; **63**: 204-10.
- RUNCIMAN JC, BOWEN-WRIGHT RM, WELSH NH, DOWNING JW. Intra-ocular pressure changes during halothane and enflurane anaesthesia. *British Journal of Anaesthesia* 1978; **50**: 371-4.
- ROSE NM, ADAMS AP. Normocapnic anaesthesia with enflurane for intra-ocular surgery. *Anaesthesia* 1980; **35**: 569-75.
- ADAMS AP, FREEMAN A, DART JKG. Normocapnic anaesthesia with trichloroethylene for intra-ocular surgery. *Anaesthesia* 1979; **34**: 526-33.
- PRYS-ROBERTS C, KELMAN GR, GREENBAUM R, ROBINSON RH. Circulatory influences of artificial ventilation during nitrous oxide anaesthesia in man. II: Results: the relative influence of mean intrathoracic pressure and arterial carbon dioxide tension. *British Journal of Anaesthesia* 1967; **39**: 533-48.
- EGER EI. *Isoflurane (Forane): a compendium and reference*. Madison, Wisconsin: Ohio Medical Products, 1982.
- JONES RM. Clinical comparison of inhalational anaesthetic agents. *British Journal of Anaesthesia* 1984; **56**: 57S-69S.
- PERKINS ES. Hand-held applanation tonometer. *British Journal of Ophthalmology*. 1965; **49**: 591-3.
- HENVILLE JD, ADAMS AP. A co-axial breathing circuit and scavenging valve. *Anaesthesia* 1976; **31**: 257-8.
- BAIN J, SPOEREL WE. Flow requirements for a modified Mapleson D system during controlled ventilation. *Canadian Anaesthetists' Society Journal* 1973; **20**: 629-36.
- HENVILLE JD, ADAMS AP. The Bain anaesthetic system. An assessment during controlled ventilation. *Anaesthesia* 1976; **31**: 247-56.

12. MAHARAJ RJ, HUMPHREY D, KAPLAN N, KADWA H, BLIGNAUT P, BROCK-UTNE JG, WELSH N. Effects of atracurium on intra-ocular pressure. *British Journal of Anaesthesia* 1984; **56**: 459–63.
13. TATTERSALL MP, MANUS NJ, JACKSON DM. The effect of atracurium or fazadinium on intra-ocular pressure. A comparative study during induction of general anaesthesia. *Anaesthesia* 1985; **40**: 805–7.
14. AUSINSCH B, GRAVES SA, MUNSON ES, LEVY NS. Intra-ocular pressure in children during isoflurane and halothane anaesthesia. *Anesthesiology* 1975; **42**: 167–72.
15. MURPHY DF, EUSTACE P, UNWIN A, MAGNER JB. Atracurium and intra-ocular pressure. *British Journal of Ophthalmology* 1985; **69**: 673–5.
16. THEYE RA, MICHENFELDER JD. Individual organ contributions to the decrease in whole-body VO_2 with isoflurane. *Anesthesiology* 1975; **42**: 35–40.
17. CUNNINGHAM AJ. Intra-ocular pressure—physiology and implications for anaesthetic management. *Canadian Anaesthetists' Society Journal* 1986; **33**: 195–208.
18. DUNCALF D. Anesthesia and intra-ocular pressure. *Bulletin of the New York Academy of Medicine* 1975; **51**: 374–81.

Comparison of propofol and methohexitone as anaesthetic agents for electroconvulsive therapy

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Summary

Propofol was compared to methohexitone for induction of anaesthesia for electroconvulsive therapy. Seizures were significantly shorter after the use of propofol, in respect of both visible seizures and duration of cerebral electrical seizure activity. This suggests the possibility that additional treatments may be needed for the same clinical effect in psychiatric illness when propofol is used as the induction agent. Propofol was more effective than methohexitone at obtunding the hypertensive response to electroconvulsive therapy without causing significant hypotension.

Key words

*Anaesthetics, intravenous; propofol.
Electroconvulsive therapy.*

Electroconvulsive therapy (ECT) is a commonly performed procedure in patients who suffer from psychiatric illness. The usual indication is severe endogenous depression, in which it has been shown to be an effective treatment.^{1,2} Anaesthesia is required to provide loss of consciousness and muscle relaxation.

The standard drugs used are methohexitone and suxamethonium. Methohexitone is used because recovery is relatively rapid. However, recovery occurs not because of metabolism of the drug but because of redistribution within the body which leads to a decrease in the plasma concentration. Significant concentrations remain for many hours, and may cause impairment of psychomotor and mental ability for up to 24 hours after administration.³ This is particularly undesirable in patients who have ECT, as they usually return quickly to a psychiatric ward where staff levels may be low and there may be little appreciation of the prolonged effects of anaesthetic agents. The hazards are increased in outpatients, particularly as psychiatric patients may be less likely than others to comply with instructions to avoid driving, sedative drugs and alcohol.

Propofol is a recently introduced rapidly acting intravenous anaesthetic agent. It is now in widespread use especially for daycase and outpatient anaesthesia, because of its characteristic of rapid recovery from anaesthesia. Several studies have shown improved quality of recovery after propofol as compared to methohexitone.^{4,5} Thus

propofol could have useful advantages if used for ECT.

It has been shown by Maletzky⁶ that benefit from ECT is related to the duration of the electrical seizure produced. A recent study with propofol⁷ showed that behavioural seizures, that is seizures measured by observation of the duration of convulsive movements, after ECT were shorter when propofol was used than after methohexitone. However, it has been emphasised by Maletzky that seizure duration must be measured by the electroencephalogram (EEG) rather than by observation of the behavioural seizure as the electrical seizure continues for varying periods after the end of visible muscle activity.⁶ Consequently, assessment of the effect of propofol on seizure duration should be made with an EEG monitor.

ECT has been noted to cause severe cardiovascular instability with increases in arterial pressure and heart rate after treatment.⁸ This may be hazardous, as many patients who require ECT are elderly and have cardiac and cerebrovascular disease. It has also been suggested that the increase in arterial pressure contributes to cognitive defects after ECT,⁹ although this has been disputed.¹⁰ Propofol causes more cardiovascular depression than methohexitone.⁵ We wished to establish whether this would successfully obtund the hypertensive response to ECT or if unacceptable hypotension would result. The purpose of the study was to assess the suitability of propofol for use as the anaesthetic agent for ECT.

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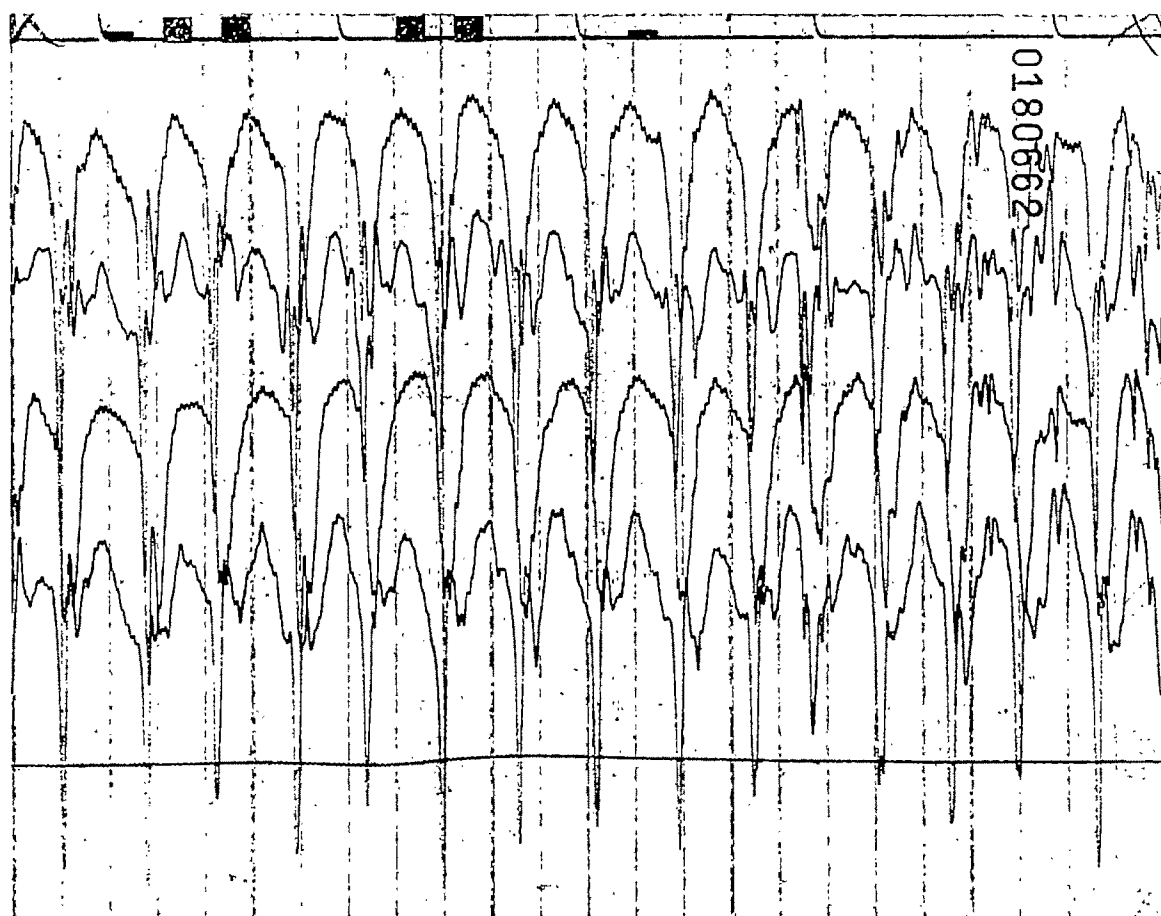


Fig. 1. EEG tracing which shows classical 'spike and wave' activity of a grand mal seizure.

Methods

Fifty patients who presented for a minimum of two ECT treatments were studied. Informed consent was obtained. Patients who required compulsory treatment under the Mental Health Act were excluded. The approval of the local University Medical Ethical Research Committee was obtained.

All patients received atropine 0.6 mg intramuscularly one hour before treatment. All had a brief medical history taken, weight and arterial pressure were measured and a physical examination was carried out as indicated. Patients were assigned randomly to receive either propofol or methohexitone 1% for their first treatment; the other drug was administered on the second occasion.

A 23-gauge needle was placed in a vein in the antecubital fossa; the intravenous induction agent was injected at a rate of 1 ml per 5 seconds until loss of the eyelash reflex occurred. Note was taken of any pain on injection or excitatory phenomena. Suxamethonium was administered in a dose of 0.6 mg/kg body weight and the patient's lungs were ventilated with 100% oxygen until muscle relaxation was established. ECT was then administered via cloth-covered electrodes soaked in potassium permanganate which were applied to standard ECT points on the temples. A standard current was administered for 3 seconds from an Ectron Duopulse machine. The same machine was used in all treatments. The patient's lungs were ventilated with 100% oxygen until the resumption of spontaneous ventilation.

An observer was assigned to time the duration of the grand mal seizure from the administration of ECT until the end of the clonic phase. Arterial pressure was measured immediately after the end of the seizure, and time taken to resumption of spontaneous respiration was noted. Cerebral electrical activity was monitored in 25 patients with an Ectromed 4640 Cerebral Function Monitor (CFM). This uses three cerebral electrodes to record a simplified EEG tracing, and detects adequately the gross derangement of cerebral electrical activity which occurs during a grand mal seizure (Figs 1 and 2). The scalp electrodes were attached to the forehead and right and left parietal regions with adhesive tape. 'ElectroGel' was placed under the electrode to maintain electrical contact. Cerebral electrical activity during therapy with ECT was recorded by the CFM on a paper printout at a paper speed of 10 cm/second and the duration of gross electrical disturbance was measured later by an observer who was blind to the treatment given. The reliability of the CFM to detect cerebral seizure activity was checked by recording simultaneously an 8-channel EEG in four patients; the cessation of 'spike and wave' activity on the EEG coincided exactly with the return of the CFM tracing to the baseline (Fig. 3).

Parametric data were analysed using a paired *t*-test. Nonparametric data were analysed using a Chi-square test.

Results

The mean age of the subjects was 53.2 years (range 22–76), and the mean weight was 64.5 kg. Twelve of the subjects

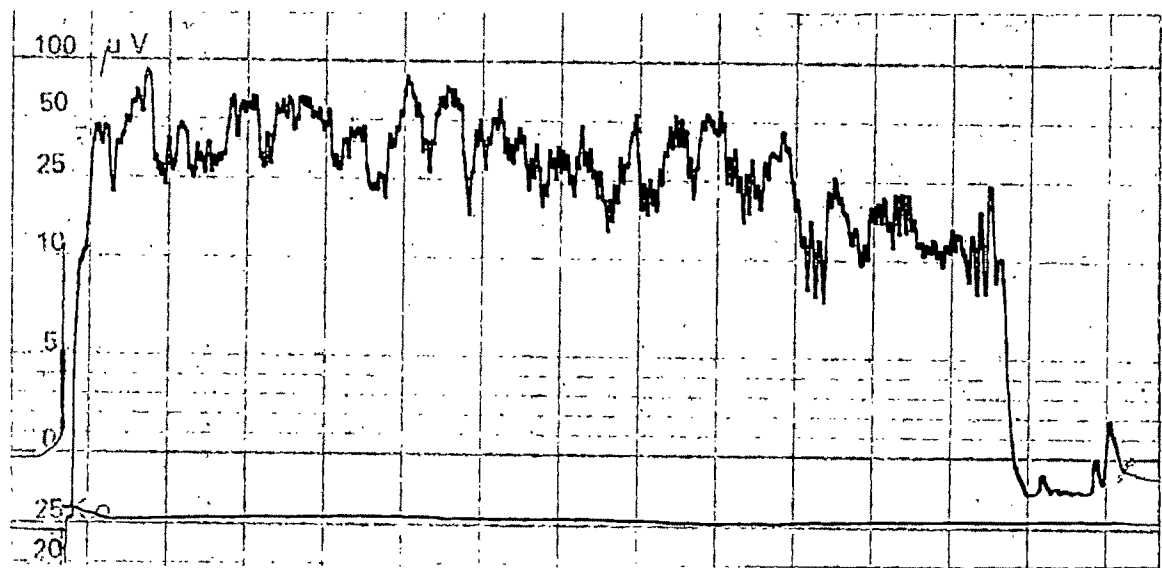


Fig. 2. Grand mal seizure after ECT as recorded on Cerebral Function Monitor.

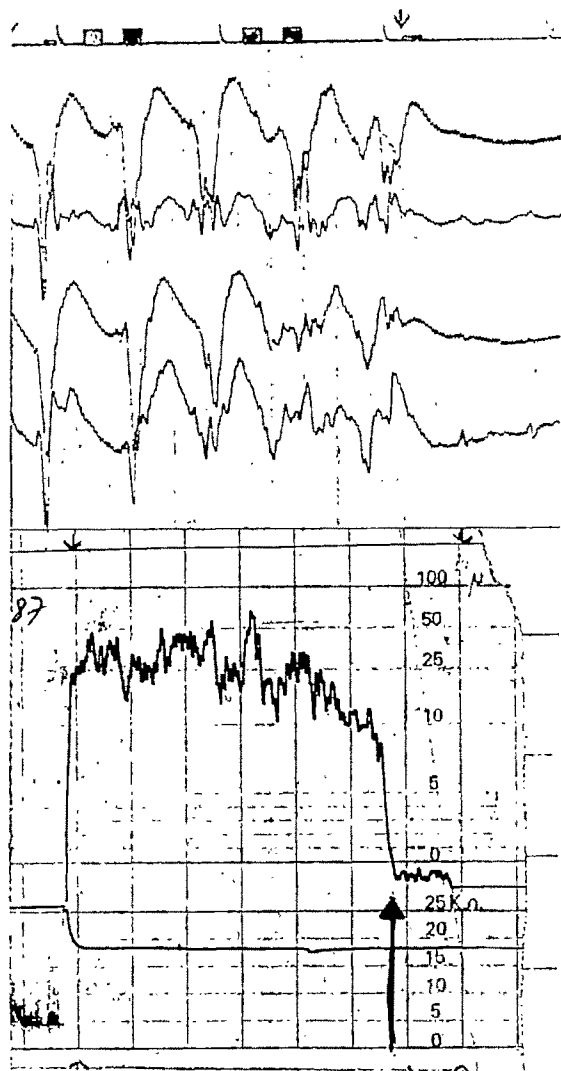


Fig. 3. EEG and CFM tracings during grand mal seizure which show simultaneous sharp end point at end of electrical seizure.

were male. The mean dose of propofol administered was 97.4 mg (1.51 mg/kg); the mean dose of methohexitone was 76.7 mg (1.19 mg/kg). Equal doses of suxamethonium were

Table 1. Mean (SD) duration, seconds, of ECT-induced behavioural and electrical seizures after propofol and methohexitone.

	Behavioural (n = 50)	Electrical (n = 25)
Propofol	23.5 (9.6)	43.2 (17.4)
Methohexitone	31.3 (15.6)	57.3 (20.3)
p	< 0.001	< 0.001

given to both groups; equal numbers had propofol and methohexitone as the anaesthetic agent for the first treatment.

The duration of seizures was significantly shorter after propofol induction than when methohexitone was used in the same patients (Table 1). This applied to both the behavioural seizures and seizures measured by CFM. Propofol was significantly better than methohexitone at obtaining the rise in arterial pressure after ECT (Table 2). It did, however, cause a significant decrease in arterial pressure in seven patients, but in no patient did systolic arterial pressure decrease below 100 mmHg. There was no significant difference between the mean duration of apnoea after propofol (212 seconds) and methohexitone (199 seconds). More unwanted effects occurred after administration of methohexitone (Table 3).

Quality of recovery after propofol has been shown to be superior to that after methohexitone^{4,5} and was not assessed in this study.

Discussion

This study confirms that propofol can be used as the induction agent for ECT. It provides smoother induction of anaesthesia than methohexitone and reduces the hypertensive response to ECT. The only disadvantage to the use of propofol in this study was the mean reduction of 25% in the duration of seizures. If the clinical effect from a course of ECT depends on the total duration of seizures, then extra treatments may be required to achieve the same therapeutic effect. For example, if a patient required seizures totalling 400 seconds for a therapeutic effect he would require seven treatments if methohexitone was used

Table 2. Effects of propofol and methohexitone on the arterial pressure after ECT.

	Increase > 20 mmHg (n = 50)	Decrease > 20 mmHg (n = 50)	Systolic arterial pressure < 100 mmHg (n = 50)
Propofol	5	7	0
Methohexitone	15	1	0
P	0.02		

Table 3. Side effects after propofol and methohexitone.

	Propofol	Methohexitone
Pain on injection	0	1
Generalised twitching	1	5
Laryngospasm	1	0

as the anaesthetic agent, but 10 if propofol was used. The risks of these extra treatments might have to be balanced against the advantages of cardiovascular stability and rapid recovery with propofol to decide which agent to use.

The Committee on Safety of Medicines recently issued a warning about the possible risk of seizures after propofol¹¹ and related this to animal work which showed that, unlike thiopentone, propofol did not protect against seizures.¹² However, seizure activity in that animal model was studied 15 minutes after administration of the drug, by which time propofol, but not thiopentone, would be substantially cleared from the bloodstream so that any anticonvulsant activity of propofol would not be apparent. The findings of the present study suggest that propofol shortens seizures to a greater extent than methohexitone.

Acknowledgments

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References

1. KENDELL RE. The present status of electroconvulsive therapy. *British Journal of Psychiatry* 1981; **139**: 265-83.
2. FREEMAN CPL, BASSON JV, CRIGHTON A. Double-blind controlled trial of electroconvulsive therapy (ECT) and simulated ECT in depressive illness. *Lancet* 1978; **i**: 738-40.
3. DUNDEE JW, WYANT GW. *Intravenous Anaesthesia*. London: Churchill Livingstone, 1974: 53.
4. MACKENZIE N, GRANT IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *British Journal of Anaesthesia* 1985; **57**: 725-31.
5. O'TOOLE DP, MILLIGAN KR, HOWE JP, MCCOLLUM JSC, DUNDEE JW. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia. *Anaesthesia* 1987; **42**: 373-6.
6. MALETZKY BM. Seizure duration and clinical effect in electroconvulsive therapy. *Comprehensive Psychiatry* 1978; **19**: 541-50.
7. SIMPSON KH, HALSALL PJ, CONN CME, STEWART KG. Seizure duration after methohexitone or propofol for induction of anaesthesia for electroconvulsive therapy (ECT). *British Journal of Anaesthesia* 1987; **59**: 1323P-4P.
8. JONES RM, KNIGHT PR. Cardiovascular and hormonal responses to electroconvulsive therapy. Modification of an exaggerated response in an hypertensive patient by β -receptor blockade. *Anaesthesia* 1981; **36**: 795-9.
9. HAMILTON M, STOCKER MJ, SPENCER CM. Post-ECT cognitive defect and elevation of blood pressure. *British Journal of Psychiatry* 1979; **135**: 77-8.
10. TAYLOR JR, KUHLENGEL BG, DEAN RS. ECT, blood pressure changes and neurophysiological deficit. *British Journal of Psychiatry* 1985; **147**: 36-8.
11. COMMITTEE ON SAFETY OF MEDICINES. Propofol. *Current Problems* 1987; 20.
12. GLEN JB, HUNTER SC, BLACKBURN TP, WOOD P. Interaction studies and other investigations of the pharmacology of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61**(Suppl. 3): 7-14.

Perineuronal morphine: a comparison with epidural morphine

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Summary

In a double-blind, randomised controlled cross-over study the effects of perineuronal (perifemoral) injections of morphine were compared with epidural injections with the same amount of morphine in patients after knee surgery. Better pain scores were achieved during treatment with epidural morphine. We have not been able to confirm the hypothesis of neuro-axonal transport of morphine from the periphery to the spinal cord.

Key words

*Analgesics, narcotics; morphine hydrochloride.
Anaesthetic techniques, regional; epidural, femoral nerve block.*

In the last few years several reports which concern neuronal blockade with morphine have been published.^{1–4} Sanchez *et al.*² injected morphine 5 mg in 10 ml saline into the neurovascular sheath of the brachial plexus of a patient suffering from a Pancoast's tumour and achieved total analgesia for 36 hours. They suggested that neuro-axonal transport of the morphine to the spinal cord was responsible for the effect. We wanted to investigate if a similar effect could be obtained with injections of morphine into the neurovascular sheath of the femoral nerve in patients with postoperative pain after knee surgery.

Methods

Ten patients aged 18–50 years scheduled for elective surgery on the knee were included in the study which was approved by the ethical committee of the hospital; all patients gave informed consent. The patients were instructed preoperatively in the use of visual analogue scales for pain estimation. They received oral diazepam, 0.25 mg/kg as premedication. Anaesthesia was induced with thiopentone and maintained with enflurane and nitrous oxide in oxygen. Pethidine was given peroperatively when needed. Atracurium was used for relaxation and was reversed after the operation with neostigmine and atropine.

An epidural catheter was placed between L₂/L₃ or L₃/L₄ after surgery but before waking. A femoral catheter was placed with the following procedure: the femoral artery was located immediately below the inguinal ligament and a 14-

gauge intravenous infusion cannula was inserted just lateral to the vessel. The femoral nerve was located accurately with a nerve stimulator and the trocar of the cannula was removed; a 16-gauge epidural catheter was passed through the cannula and advanced 6–10 cm cranially. The cannula was removed and the catheter protected with a bacterial filter. The technique of placing the femoral catheters had been verified previously using injections of contrast medium.

The patients were observed for 48 hours postoperatively. Morphine was administered via the femoral or epidural catheters in a randomised double-blind cross-over fashion. In the first 24 hours they received either morphine 4 mg in saline 10 ml epidurally or via the femoral catheter. The treatment was reversed for the next 24 hours. Blinded ampoules were used and treatment was started when the patients arrived in the recovery room. Injections were repeated 6-hourly. All patients received paracetamol 1g four times daily. Supplementary injections of morphine 0.125 mg/kg intramuscularly were given on demand except during the first 6 hours when 2.5 mg doses were given intravenously on demand.

A linear visual analogue scale going from 0 (no pain) to 100 mm (the worst pain imaginable) was used to estimate pain intensity. Pain scores were recorded on arrival in the recovery room and then every 4 hours throughout the study. The number of times patients vomited was registered and an evaluation of nausea was performed at 24 and 48 hours; the patients categorised their nausea as: 'none to slight' or 'some to severe'. The degree of difficulty with

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Table 1. Patient and operative data.

Patient	Sex f/m	Age (years)	Weight (kg)	Height (cm)	Duration of operation (minutes)	Peroperative pethidine consumption (mg)
1	f	22	63	172	135	120
2	f	22	61	174	30	80
3	f	22	55	157	210	105
4	m	23	65	175	225	120
5	f	23	67	172	120	130
6	m	31	70	179	150	75
7	m	41	63	172	90	80
8	f	48	62	168	45	100
9	f	31	84	172	75	135
10	m	19	70	180	120	105
Median		23	64	173	120	105
Range		19–48	55–84	157–180	30–225	75–135

Table 2. Median visual analogue scores (VAS) and supplementary morphine consumption during the two different treatments.

Treatment	Epidural morphine	Femoral morphine	
Median VAS scores	9	33	$p < 0.05$
Median supplementary morphine consumption mg/kg/24 hours	0.06	0.27	$p > 0.05$

micturition was noted as was the need for catheterisation of the bladder and the frequency of itching.

Statistical methods

Statistical analyses were performed using the Wilcoxon two-sample test to compare visual pain scores and the use of supplementary morphine. The sign test was used to compare side effects. Data were tested for period- and carry-over effects according to Grizzle⁵ and Hills and Armitage.⁶

Results

Patient and operative data are shown in Table 1. Seven patients were operated on for rupture of one of the cruciate ligaments of the knee and three for recurrent subluxation of the patella.

Six patients were administered epidural morphine in the first 24 hours and perifemoral morphine the next 24 hours and four patients were treated in the reverse order. The median pain score just after arrival in the recovery room was 53 mm (range 38–84 mm). Treatment with perifemoral morphine was associated with a significantly greater median pain score than during treatment with epidural morphine, 33 mm (0–82) and 9 mm (0–49) respectively, ($p < 0.05$, Table 2). Neither period- nor carry-over effects were found to influence the results. Supplementary median morphine consumption was 0.27 mg/kg/24 hour (0–0.64 mg/kg/24 hour) during treatment with perifemoral morphine and 0.06 mg/kg/24 hour (0–0.48 mg/kg/24 hour) during epidural treatment. This difference was not significant ($p > 0.05$). Differences between treatments with regard to side effects were not found to be significant, though it seemed that the epidural morphine patients had a higher tendency to nausea and vomiting.

Discussion

The main effects of opioids on primary afferent transmission are most likely exerted within the central nervous system. The spinal effects of opioids are believed to result from an action on the neuronal transmission in the dorsal horn, the gelatinous substance, and linked with the occupation of opiate receptors.⁷

There are, however, indications of peripheral effects of opioids. Opioid binding has been demonstrated in the axons and ganglia of primary afferents,⁸ and a direct action on peripheral nerve endings of primary afferents has been postulated.^{9,10} Furthermore intrathecal pethidine in high concentrations has been shown effective as a sole agent for surgery,¹¹ which was interpreted as a combined local anaesthetic and opioid effect. Perineuronal injections of morphine have relieved pathological pain in humans at a dosage and under conditions where systemic morphine effects could be ruled out.⁴

The neuro-axonal transport of perineuronal injected morphine to the dorsal horn has been suggested as a possible way to explain unexpected effects.^{1,2} This hypothesis has not been subjected to a controlled trial and the present study was undertaken to investigate the problem under clinical conditions. In our experience, patients after exploratory operations on the knee suffer from considerable pain in the first 2 days postoperatively. Peripheral blockade with local anaesthetics which correspond to the segments L_{2–4} (3 in 1 block) has been shown to be effective in earlier studies both in respect of peroperative and postoperative pain.^{12,13} If the theory about neuroaxonal transport of morphine was to be correct then injections of morphine in the neurovascular sheath around the femoral nerve should be effective in the treatment of postoperative pain, which arises from the region innervated by the femoral nerve. We have chosen epidural morphine as our control group because we know that the pain-killing effect here originates mainly from an action on the substantia gelatinosa of the spinal cord.

We found significantly better effects from epidural morphine compared to femoral. The lowest amount of supplementary morphine was found in the epidural morphine group but the difference in supplementary doses was not significant, probably due to the small number of patients in the study. It has been shown a number of times that the interindividual perception of pain and the need of analgesics varies a great deal.¹⁴ A crossover design was therefore thought to be the most suitable, though it has

the risks of period- and carry-over effects, but this did not make any difference in this study.

The cerebrospinal fluid (CSF) levels of morphine after epidural injection exceed those in plasma after 15 minutes and remain above 20 ng/ml for as long as 20 hours after the injection of 2 mg of epidural morphine.^{15,16} Peak concentrations are delayed compared with plasma levels and occur 1–4 hours after injection. Nordberg and co-workers¹⁶ found a pronounced variability in CSF concentrations after intramuscular administration of morphine, but in general the CSF concentrations were lower and showed a delayed uptake compared to plasma. Maximum concentrations in CSF were found after 3 hours and amounted to 90% of plasma levels at the time of apparent equilibrium.

We did not find any evidence of clinically significant neuro-axonal transport of morphine from the periphery to the spinal cord. Our results are compatible with those found by Bullingham *et al.*¹⁷ who also failed to obtain any pain relief with perineuronal morphine used for ankle block. Recently it has been demonstrated, under laboratory conditions, that preservative-free morphine does not alter the response in nociceptive fibres when applied directly to the nerve fibre.¹⁸

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References

1. MOCVERO G. Analgesia selettiva con morfina perinervosa. *Incontri Di Anestesia, Rianimazione e Scienze Affini* 1981; 16: 1–3.
2. SANCHEZ R, NIELSEN H, HESLET L, IVERSEN AD. Neuronal blockade with morphine. A hypothesis. *Anaesthesia* 1984; 39: 788–9.
3. NIELSEN H, SANCHEZ R, KNUDSEN F. Perineuronal morphine for the relief of chronic pain. *Anaesthesia* 1986; 41: 768–9.
4. MAYS KS, LIPMAN JJ, SCHNAPP M. Local analgesia without anesthesia using peripheral perineuronal morphine injections. *Anesthesia and Analgesia* 1987; 66: 417–20.
5. GRIZZLE JE. The two-period change-over design and its use in clinical trials. *Biometrics* 1965; 21: 467–80.
6. HILLS M, ARMITAGE P. The two-period cross-over clinical trial. *The British Journal of Clinical Pharmacology* 1979; 8: 7–20.
7. YAKSH TL, NOUEHED R. The physiology and pharmacology of spinal opiates. *Annual Review of Pharmacology and Toxicology* 1985; 25: 433–62.
8. FIELDS HL, EMSON PC, LEIGH BK, GILBERT RFT, IVERSEN LL. Multiple opiate receptor sites on primary afferent fibres. *Nature* 1980; 284: 351–3.
9. FERREIRA SH, NAKAMURA M. II; Prostaglandin hyperalgesia: the peripheral analgesic activity of morphine, enkephalins and opioid antagonists. *Prostaglandin* 1979; 18: 191–200.
10. NINCOVIC M, HUNT SP, GLEAVE RJN. Localisation of opiate and histamine H₁-receptors in the primate sensory ganglia and spinal cord. *Brain Research* 1982; 241: 197–206.
11. ACALOVSKI I, ENE V, LORINCI E, NICOLAUS F. Saddle block with pethidine for perineal operations. *British Journal of Anaesthesia* 1986; 58: 1012–6.
12. PATEL NJ, FLASHBURG MH, PASKIN S, GROSSMAN R. A regional anesthetic technique compared to general anesthesia for outpatient knee arthroscopy. *Anesthesia and Analgesia* 1986; 65: 185–7.
13. ROSENBLATT RH. Continuous femoral anesthesia for lower extremity surgery. *Anesthesia and Analgesia* 1980; 59: 631–2.
14. DAHLSTRØM B, TAMSEN A, PAALZOW L, HARTVIG P. Patient-controlled analgesic therapy Part 4: pharmacokinetics and analgesic plasma concentrations of morphine. *Clinical Pharmacokinetics* 1982; 7: 266–79.
15. NORDBERG G, HEDNER T, MELLSTRAND T, DAHLSTRØM B. Pharmacokinetic aspects of epidural morphine analgesia. *Anesthesiology* 1983; 58: 545–51.
16. NORDBERG G. Pharmacokinetic aspects of spinal morphine analgesia. *Acta Anaesthesiologica Scandinavica* 1984; (Suppl. 79).
17. BULLINGHAM R, O'SULLIVAN G, MCQUAY H, POPPLETON P, ROLFE M, EVANS P, MOORE A. Perineuronal injection of morphine fails to relieve postoperative pain in humans. *Anesthesia and Analgesia* 1983; 62: 164–7.
18. SENAMI M, AOKI M, KITAHATA LM, COLLINS JG, KUMETA Y, MURATA K. Lack of opiate effects on cat c polymodal nociceptive fibres. *Pain* 1986; 27: 81–90.

Hypnosis and daycase anaesthesia

A study to reduce pre-operative anxiety and intra-operative anaesthetic requirements

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Summary

Fifty-two female patients who underwent gynaecological operations as day cases received either a short pre-operative hypnotic induction or a brief discussion of equal duration. Hypnotised patients who underwent vaginal termination of pregnancy required significantly less methohexitone for induction of anaesthesia. They were also significantly more relaxed as judged by their visual analogue scores for anxiety. Less than half of the patients were satisfied with their knowledge about the operative procedure even after discussions with the surgeon and anaesthetist. A significant correlation was found between anxiety and perceived knowledge of procedures. The results suggest that pre-operative hypnosis can provide a quick and effective way to reduce pre-operative patient anxiety and anaesthetic requirements for gynaecological daycase surgery.

Key words

Hypnosis.

Surgery; gynaecological, daycase.

There is an increase of interest in the psychological preparation of patients for surgery. Most studies have used postoperative measures: analgesic requirements, length of hospital stay and patient satisfaction. Pre-operative interventions designed to increase patient understanding, reduce anxiety and aid recovery have included films, modelling, brochures, counselling, group discussions and hypnosis.^{1–6} In a meta-analysis of 34 controlled studies the use of psychological interventions was examined on pre-operative surgical patients and patients who had suffered myocardial infarction.⁷ A reduction in the experimental group's stay in hospital by approximately 2 days was recorded, which suggested that physical, psychological and economic benefits may accrue from such interventions.

The examination of pre-operative influences upon post-operative variables is useful, but few studies have investigated the influence of pre-operative psychological variables upon intra-operative factors such as anaesthetic requirements. A reduction in either anxiety or medication might also prove clinically useful, as pre-operative anxiety is generally an indication of need for increased analgesia and anaesthesia, and often a signal for a difficult induction. Daycase surgery is known to provoke pre-operative anxiety, and although the operations may be minor, the

patient's level of anxiety often is not. Premedication is not given routinely to day cases.

The present research project sought to answer the following questions: are hypnosis or a discussion of similar length equally effective ways to reduce pre-operative anxiety; does reduced anxiety result in decreased intra-operative anaesthetic requirements; and do pre-operative psychological factors predict higher anaesthetic requirements?

Methods

Fifty-three women, average age 24.6 years, who were to have elective gynaecological surgery in the Day Surgery Unit at Addenbrooke's Hospital, Cambridge, were interviewed individually by a consultant or senior registrar anaesthetist and then escorted by a nurse to a communal waiting area. Each patient was called in turn to be interviewed by a psychologist. The interviews lasted an average of 8 minutes, after which the patient was brought into the operating theatre. This eliminated any opportunity for discussion between patients. The elements of the interview are described below.

Explanation of the study and written consent. The patients

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were told the aims of the study and any questions were answered.

*Taylor Manifest Anxiety Scale.*⁸ The Taylor Manifest Anxiety Scale is a measure of state anxiety.

Linear analogue anxiety scale. The linear analogue scale was an unmarked 100 mm line with one end labelled 'anxious' and the other 'relaxed'. Patients were asked to put a tick anywhere along the line which corresponded to how relaxed or anxious they felt at that moment.

Structured interview. The structured interview consisted of the questions shown in Table 1.

Table 1. Questions in structured interview.

What operation are you having performed?
What do you know about it?
Has anyone in your family or a close friend had a similar operation?
How would you describe your visit with the anaesthetist?
Were there any areas discussed that you found especially informative?
Were there any areas discussed that you found uninteresting?
Did you find that talking to the anaesthetist made you more or less nervous?
How well was the anaesthetic procedure explained?
Was there anything you found confusing or unclear?
Did the anaesthetist speak to you in an understandable fashion or were there a lot of technical terms?
Do you know the name of the anaesthetist?
Other than putting you to sleep, do you know the role of the anaesthetist?

Answers were scored as either yes/no or on a four point scale, as appropriate to the question.

Short discussion or hypnosis. The structured interview was followed either by a short discussion which drew upon some aspect of the patient's life that had been mentioned or by hypnosis. Assignment to groups was randomised. Hypnosis was presented to the patient as a technique which could help her relax. She was told that 'patients often find it useful and helpful to be as relaxed as possible before their operations'. A modification of Elman's hypnotic technique⁹ was employed which lasted about 3 minutes. The patient was told before the end of the hypnosis that she could re-experience the same sense of relaxation as soon as she lay down on the operating table.

Second linear analogue anxiety scale. A second linear analogue anxiety scale was marked after the discussion or hypnosis.

Anaesthesia

Anaesthesia was induced in the operating theatre by one of three anaesthetists, blind to the experimental condition. No premedication was prescribed. Alfentanil 7.5 µg/kg was administered immediately before an induction dose of methohexitone 1.5 mg/kg. Supplementary doses of methohexitone 0.25 mg/kg were administered as necessary. Operations lasted less than 15 minutes. The patients breathed oxygen 5 litres/minute spontaneously via an MC mask.

Results

All but one of the patients completed the study and no patient refused to participate. The following operations

were performed: dilatation and curettage, $n = 17$ (32%); vaginal termination of pregnancy (VTOP), $n = 27$ (51%); and other procedures, $n = 9$ (17%).

Initial assessment of anxiety

The mean patient score on the Taylor Manifest Anxiety Scale was 7.5 (SD 3.8). On the visual analogue scale, the mean was 43.6 (SD 24.8). There was no significant difference in anxiety state between patients who underwent VTOP and the rest of the sample as measured on the visual linear analogue scales.

Knowledge

Thirty-six percent of the patients stated that they had no knowledge of their operation, 21% poor, 15% some, and 26% fair to good knowledge. Forty-eight percent of patients did not know whether a member of their family or a friend had had a similar operation. Twenty-two percent of the women reported that they knew of at least one family member or close friend who had had a similar procedure. A small but significant negative correlation was found between perceived knowledge and initial anxiety scores on the Taylor Manifest Anxiety Scale ($r = -0.28$, $p < .03$), which indicated that less anxiety was reported by more knowledgeable patients.

The anaesthetist's visit

Twenty-nine percent of the patients described their visit with the anaesthetist as poor, 30% fair, 32% good, and 9% excellent. Sixty-four percent found the interview to be informative. Only 4% found that issues discussed were of no interest to them. Seventeen percent of the patients felt that they had been made more anxious by the interview. Forty-five percent were made less anxious and 38% reported no change.

Almost half the patients were dissatisfied (47%) with the explanation of anaesthetic procedures, while 38% were pleased. Only in 4% of the cases did the patient report that she knew the procedures to her satisfaction. Nine percent of patients reported that what they had been told confused them or was unclear. This is supported by the fact that 77% of patients reported that the anaesthetist spoke in a nonconfusing and understandable manner. Only 52% of the patients knew the role of the anaesthetist other than putting them 'to sleep'. Seventy-nine percent knew the anaesthetist's name. Many women spontaneously related that the procedures were poorly explained in terms of depth and detail. The most frequently asked question at the end of the interview was whether induction would be via a needle or a mask. The majority of women said that the most informative part of the interview with the anaesthetist was to be told the length of the operation.

Hypnosis

Twenty-five patients received hypnosis (experimental group) and 27 participated in a discussion. One patient was called to surgery during the interview and was therefore excluded from the study. Anxiety scores are presented in Table 2. No significant differences were found on either measure of anxiety state between the groups prior to

Table 2. Mean anxiety (SD) scores of patients who received hypnosis or discussion.

	Hypnosis	Discussion
	<i>n</i> = 25	<i>n</i> = 27
Taylor manifest anxiety score	7.8 (3.9)	7.0 (3.7)
Visual analogue scale (anxiety), mm	43.7 (24.4)	43.4 (25.4)
Visual analogue scale (anxiety) after hypnosis or discussion, mm	23.9 (20.1)*	46.5 (27.9)

* $p < 0.01$ between hypnosis and discussion groups.

induction: experimental group, mean Taylor Manifest Anxiety score 7.8 (SD 3.9); linear analogue anxiety score 43.7 (SD 24.4); controls, Taylor Manifest Anxiety score 7.0 (SD 3.7); linear analogue anxiety score 43.4 (SD 25.4). The hypnosis group had a mean anxiety score of 23.9 (SD 20.1), and the control group, 46.5 (SD 27.9), after hypnosis or the brief discussion. The difference between analogue relaxation scores of the groups ($F = 1.93$) was significant at a level of $p < .01$.

Anaesthesia

Thirty patients received only methohexitone and alfentanil. These included 14 who underwent VTOP; seven of these patients were hypnotised. This afforded the opportunity to ascertain whether hypnosis had a differential effect upon anaesthetic or analgesic requirements for a single surgical procedure. No significant difference was found in the mean dose of alfentanil: the hypnosis group received 435 µg, and the controls 500 µg. However, hypnotised patients required significantly less methohexitone (137 mg; SD 25.8) than the control group (171 mg; SD 30.1). ($F = 1.36$, $p < .03$). This suggests that hypnosis can decrease intra-operative anaesthetic requirements.

Both perceived knowledge and the initial assessment of pre-operative anxiety appeared to correlate with the amount of methohexitone required, but this relationship was not statistically significant.

Discussion

Many patients feel anxious and poorly informed before operations which medical staff often consider to be routine. This is particularly true for women who undergo gynaecological procedures such as termination of pregnancy, where additional, difficult psychological issues are often brought to the fore.

Specific fears have been associated with both general anaesthesia and surgery. These include death, mutilation, and loss of control. Ramsay¹⁰ assessed 382 general surgical patients and found 73% fearful. Anaesthesia was feared by 62%, and surgery by 11%. Twenty-three percent of these patients had a variety of fears which ranged from cancer to the unknown. Age was a significant factor; children and the elderly expressed less fear. Type of operation was also a significant factor while gender was not; 30% of patients with peptic ulcer and 100% of women with a breast lump were fearful. Modell and Guerra¹¹ reported that 85% of patients felt anxious before surgery. In the present study over two-thirds of patients who underwent VTOP did not know whether a relative or friend had undergone a similar procedure. This may reflect the fact that these procedures

are not discussed openly, so that the women's feelings of isolation, ignorance and anxiety are increased.

Complicating factors include the transparency of instruments designed to measure anxiety and the desire on the part of many patients to appear courageous and compliant. Duff and Hollingshead¹² wrote in this regard: 'The patient often informs the physician selectively, describing his physical symptoms but not his emotional state, since it (is) acceptable, though unpleasant, to be physically ill, but not acceptable to be mentally ill.' Failure to conform to the role of 'good patient' may therefore lead to a minimisation of fears.¹³

One third of the women in the present study stated that they had no understanding of the operation. This followed their discussions with both the surgeon and anaesthetist. A question arises as to whether they indeed wished to know more or felt unable to obtain the desired information. It is unlikely that they did not want the information, as many of these same women complained about the lack of detail in the explanations.

The provision of information does not have a uniformly positive effect. Patients may either wish to be informed about the details of their operation, remain uninformed, or a mixture of both. As the patient role often makes it difficult for them to assert their desires (and staff may not ask), this right to know or right not to know may be violated. A desire to allay patient fears may create some where none existed before. The significant relationship between perceived knowledge and anxiety in this study suggests that the more knowledge patients feel they have (which may be positively correlated with actual knowledge, although this is impossible to assess from the present data) the less anxiety is displayed. Consequently, many, but not all patients, would appear to benefit from a factual discussion or written information provided it is not too technical. This is true for children as well as adults. Pinkerton¹⁴ wrote: '... Even one exposure to detailed pre-operative briefing was apparently of greater benefit than a show of nonspecific kindness, even though many of these patients, because they were so young, might well have been expected to respond more to cossetting than to factual explanation'.

Seventy percent of patients in Modell and Guerra's study said they had been made less nervous by the anaesthetist's visit, while 17% reported that the visit had increased their anxiety.¹¹ In the present series 50% of the women found that the visit with the anaesthetist had made them less anxious. This coincides with the finding that the pre-operative visit alone, without the inclusion of particular psychological measures, was as effective in reducing anxiety as a premedication.¹⁵ It is unclear which factors inherent in the visit with the anaesthetist are responsible for this effect: expectation, motivation, information, reassurance, rapport, suggestions, or the knowledge that the operation is close at hand. It is equally unclear which factors increase some patients' anxieties. The visit with the anaesthetist can mitigate anxiety, but this study suggests that it can be further reduced. In the case where it has been elevated, a simple intervention may be uniquely useful.

The degree to which a particular psychological intervention, such as hypnosis, can help patients to cope with their operation depends not only upon the operation and patient subgroup, but also upon individual patient characteristics

such as motivation, compliance, locus of control, and reactions to pain. It is unlikely that any one technique will be ideal for all patients. However, techniques such as hypnosis which can relax patients quickly without major side effects may have a role in reducing pre-operative anxiety, may influence intra-operative factors, and might enhance recovery.

Hypnosis has been shown to be an effective analgesic and anxiolytic in both laboratory and hospital settings. It is not used routinely in the pre-operative period because of the perception that it is both time consuming and requires a highly skilled hypnotist. However, hypnotic inductions can be quick and the skills can be taught easily to medical and nonmedical staff. Hypnosis in this study appeared to be uniformly beneficial. None of the patients reported feeling more anxious after termination of hypnosis than before. The patient's motivation to comply and relax may have added to its success. Time did not allow the administration of standardised tests of hypnotic depth. It may be interesting in future studies to assess whether deeply hypnotised patients require less anaesthetic. More careful studies are planned to test this hypothesis.

Conclusion

It is clear from these results that hypnosis, or a similar procedure that can be used to relax patients during a pre-operative interview, can both mitigate the patient's feelings of anxiety and reduce anaesthetic requirements. As one of the aims of outpatient surgery is to achieve street fitness as quickly as possible a reduction in the amount of anaesthetic, even of a small amount, may be beneficial. In addition, patients who feel more relaxed may face their operations more optimistically and might recover more quickly.

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References

1. VERNON DTA, BAILEY WC. The use of motion pictures in the psychological preparation of children for the induction of anaesthesia. *Anesthesiology* 1974; **40**: 68-72.
2. VERNON DTA. Use of modelling to modify children's responses to a natural, potentially stressful situation. *Journal of Applied Psychology* 1973; **58**: 351-6.
3. FINESILVER C. Preparation of adult patients for cardiac catheterization and coronary cineangiography. *International Journal of Nursing Studies* 1978; **15**: 211-21.
4. SURMAN OS, HACKETT TP, SILVERBERG EL, BEHRENDT DM. Usefulness of psychiatric intervention in patients undergoing cardiac surgery. *Archives of General Psychiatry* 1974; **30**: 830-5.
5. FIELD PB. Effects of tape-recorded hypnotic preparation for surgery. *International Journal of Clinical and Experimental Hypnosis* 1976; **22**: 54-61.
6. KOLOUCH FT. Hypnosis and surgical convalescence: A study of subjective factors in postoperative recovery. *American Journal of Clinical Hypnosis* 1964; **7**: 120-9.
7. MUMFORD E, SCHLESINGER HJ, GLASS G. The effect of psychological intervention on recovery from surgery and heart attacks: an analysis of the literature. *American Journal of Public Health* 1982; **72**: 141-51.
8. TAYLOR J. A personality scale of manifest anxiety. *Journal of Abnormal and Social Psychology* 1953; **48**: 285-90.
9. ELMAN D. *Hypnotherapy*. Glendale, California: Westwood, 1970.
10. RAMSAY MAE. A survey of pre-operative fear. *Anaesthesia* 1972; **27**: 396-402.
11. MODELL JG, GUERRA F. Psychological problems in the surgical patient. In: GUERRA F, ALDRETE JA, eds. *Emotional and psychological responses to anaesthesia and surgery*. New York: Grune and Stratton, 1980.
12. DUFF R, HOLLINGSHEAD A. The organization of hospital care. In: DREITZEL HP, ed. *The social organization of health*. New York: Macmillan, 1971: 238.
13. TAGLIACCOZZO DL, MAUKSCH HD. The patient's view of the patient's role. In: JACO EG, ed. *Patients, physicians, and illness*. London: Collier-Macmillan, 1972: 162-76.
14. PINKERTON P. Preventing psychotrauma in childhood anaesthesia. In: REES GH, GRAY TC, eds. *Paediatric anaesthesia*. London: Butterworth, 1981: 1-18.
15. EGBERT LD, BATTIT GE, TURNDORF H, BEECHER HK. The value of the preoperative visit by an anesthetist. A study of doctor-patient rapport. *Journal of the American Medical Association* 1963; **185**: 553-5.

A comparison of two anaesthetic techniques for daycase arthroscopy

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Summary

A randomised, double-blind study of 100 patients admitted for daycase arthroscopy was undertaken. Fifty patients received alfentanil 500 µg and midazolam 5 mg, and 50 received alfentanil 500 µg alone, in each case 2 minutes before induction of anaesthesia with methohexitone. Anaesthesia was maintained in both groups with nitrous oxide, oxygen and enflurane. Recovery was assessed quantitatively by measuring time to when they awoke and by a comparison of pre- and postoperative performance of p-deletion and postbox tests. Qualitative assessment of recovery and of postoperative pain was also undertaken. Patients completed a questionnaire to record the incidence of any anaesthetic-related symptoms on the first and second postoperative days. Patients who received midazolam required a reduced dose of methohexitone but their initial recovery time was prolonged significantly. The incidences of anaesthetic-related side effects and postoperative pain were similar in the two groups and while the questionnaires did not reveal any statistically significant differences in symptoms on the first 2 postoperative days, the results indicated that patients who received a larger induction dose of methohexitone were subjectively drowsier on the first day after operation.

Key words

Premedication; alfentanil, midazolam.

Recovery.

Patients admitted for daycase surgery pose particular problems for the anaesthetist. In common with all patients who await surgery, they suffer from a variety of degrees of fear and anxiety. The administration of appropriate premedication would help to allay such anxiety and also reduce the doses of anaesthetic agents required both to induce and maintain anaesthesia. The short-acting anxiolytic agent temazepam has been shown to allay anxiety and to reduce anaesthetic requirement and postoperative morbidity without prolonging recovery time.^{1,2} However, there are logistical difficulties associated with the organisation of oral premedication for patients who may be admitted to a busy day-surgery ward only a short time before the induction of anaesthesia. It has become common practice in our hospital for such patients to be given small doses of midazolam and alfentanil prior to induction of anaesthesia, in the hope that this pretreatment might reduce the dose of induction agent necessary and thus provide a shorter and more pleasant recovery. Such an outcome would have potential advantages in that postoperative morbidity might be reduced, and a more rapid turnover of patients might result, with more efficient use of beds. We therefore conducted a study to examine the quality of anaesthesia and recovery in patients who were

scheduled to undergo daycase arthroscopy, and who were either pretreated with a combination of midazolam and alfentanil or received alfentanil alone.

Patients and methods

One hundred patients between the ages of 15 and 63 years who were admitted to the day unit for arthroscopic examination and in some cases arthroscopic surgery of the knee, took part in the study which was approved by the local ethical committee. All the patients were fit apart from their orthopaedic condition and all gave informed consent.

The patients were allocated randomly to one of two groups; a midazolam group (Group M) and a saline group (Group S). A 23-gauge cannula was inserted into an ante-cubital fossa vein when the patient arrived in the anaesthetic room, and 500 µg of alfentanil was administered either with midazolam 5 mg (Group M) or 1 ml of sodium chloride 0.9% (Group S). The midazolam and saline were prepared in unmarked coded ampoules and the anaesthetist was not aware which solution was being given. Exactly 2 minutes after this injection, the patients received a dose of methohexitone 1% given at a rate of 1 ml per 3 seconds until the eyelash reflex was obtunded. The dose of meth-

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oxitane was noted and the patient was asked whether the administration of the drug was in any way painful or uncomfortable. The incidence of any hiccup or spontaneous muscle movement was also noted. Anaesthesia was maintained with nitrous oxide, oxygen and enflurane 4% until the arthroscope was inserted; the concentration of enflurane was then reduced to 1% until the procedure was completed. The nitrous oxide and enflurane were discontinued at the time that the skin sutures were inserted and 100% oxygen was administered. The time taken from the end of anaesthesia until the patient was sufficiently conscious to give his or her own name correctly on request, was noted.

Postoperative pain was treated either with papaveretum by intramuscular injection or by oral administration of a combination of papaveretum and aspirin, depending on its severity. Nausea was treated with metoclopramide 10 mg intramuscularly. Two tests were used to assess recovery. The first, based on the pegboard test described by Vickers,³ involved the use of a Kiddicraft postbox toy.⁴ Eighteen shapes of three different types were available to 'post' through the lid of the toy; the time taken to post all 18 shapes was noted. The second test was the letter p deletion test, described by Dixon and Thornton.⁵ The patient was presented with a foolscap sheet which contained 58 lines of 36 close-spaced random letters and asked to delete as many letters p as possible without omission in 3 minutes. The number of lines so completed was noted.

These two tests were performed before operation and at one hour and 2 hours after the end of anaesthesia. The magnitudes of pain, nausea, headache, sleepiness and dizziness at these times were noted, each on a three-point scale: 0, absent; 1, moderate; 2, severe. The need for analgesic or antiemetic medication in the immediate postoperative period was recorded.

Questionnaire

All patients were given a questionnaire to take home. They were asked to complete it on the morning after their operation and again on the morning of the second day after operation. Questions were asked about the presence of nausea, headache, pain, sleepiness or dizziness, again on a three-point scale of 0, none; 1, a little; or 2, a lot. Patients were also asked to record the number of pain-killing tablets taken since they left the hospital and whether, apart from residual discomfort or disability in the affected knee, they felt able to resume their normal daily activities. They were then asked to return the completed questionnaire to the hospital in the stamped, addressed envelope provided.

Results

The 50 patients in each group were comparable in respect of age and weight (Table 1). There were 27 males and 23 females in each group. None of the patients complained of any pain on injection of alfentanil, saline, midazolam or methohexitone. There was no incidence of hiccup, nausea or muscle twitching during induction of anaesthesia in any patient. The mean induction dose of methohexitone was significantly less in Group M ($p < 0.05$); it was less than half that in Group S (Table 1). Five patients, all in Group M, required no methohexitone at all.

Table 1. Patient age, weight, duration of anaesthesia, dose of methohexitone and waking time. Values expressed as mean (SEM).

	Group S	Group M
Age, years	32.0 (1.7)	30.1 (1.4)
Weight, kg	69.3 (1.7)	69.8 (1.7)
Duration, minutes	39.8 (2.0)	33.7 (1.1)
Methohexitone, mg	76.9 (3.8)	33.3 (2.6)
Waking time, minutes	6.4 (0.3)	9.5 (0.6)

The mean duration of anaesthesia in the study as a whole was 36.7 minutes but was significantly shorter in Group M than in Group S (Table 1). However, the mean time taken from the end of anaesthesia for patients to give their full name correctly was less in Group S (6.4 minutes) than in Group M (9.5 minutes; $p < 0.05$). Forty-six percent of patients in Group S were able to give their name within 5 minutes of the end of anaesthesia and 94% within 10 minutes, compared with 16% and 64% respectively in Group M.

Tables 2 and 3 show the results of the p-deletion and postbox tests performed before and after operation. Three patients (6%) in Group M and six patients (12%) in Group S did not feel well enough to perform the tests at one hour postoperatively. The performance of the

Table 2. Results of p-deletion tests. Values expressed as mean (SEM).

	Group S	Group M
Before operation	32.4 (1.1)	35.5 (1.3)
After operation, 1 hour	29.3 (1.3)	28.2 (1.3)
After operation, 2 hours	32.6 (1.3)	33.1 (1.3)

Table 3. Results of postbox tests in seconds. Values expressed as mean (SEM).

	Group S	Group M
Before operation	21.5 (0.5)	22.0 (0.6)
After operation, 1 hour	24.7 (0.8)	27.5 (1.0)
After operation, 2 hours	22.4 (0.6)	23.9 (0.8)

p-deletion tests was significantly worse in both groups at one hour after operation compared with the results before operation, but by 2 hours there were no differences. Patients in Group M performed this test significantly less well at one hour than did those in Group S ($p < 0.05$). The postbox tests were performed less well by both groups after one and 2 hours compared with the pre-operative figures. Patients in Group M did significantly less well at both one hour and 2 hours postoperatively than did those in Group S ($p < 0.05$).

Almost twice as many patients in Group M (60%, compared with 34% in Group S) felt moderately sleepy after one hour (Table 4). However, the incidence of moderate sleepiness at 2 hours was almost identical in both groups. The six patients in the midazolam group and the three patients in the saline group who were very sleepy after one hour were the same patients who could not perform the p-deletion and postbox tests at that time.

There were no significant differences between groups in the incidences of dizziness and headache during the recovery period. There was a low incidence of postoperative nausea in the study as a whole, with the prevalence slightly higher in Group S (Table 4). Only four patients required antiemetic medication, three in Group S and one in Group M. The

Table 4. Incidence of side effects. Number of patients affected. 1, moderate; 2, severe.

		Group S	Group M
Nausea, 1 hour	1	2	2
	2	3	1
Nausea, 2 hours	1	3	2
	2	0	0
Sleepiness, 1 hour	1	17	30
	2	6	3
Sleepiness, 2 hours	1	6	7
	2	1	1
Dizziness, 1 hour	1	6	7
	2	3	1
Dizziness, 2 hours	1	1	1
	2	1	0
Headache, 1 hour	1	4	5
	2	2	1
Headache, 2 hours	1	0	2
	2	1	1

Table 5. Severity of pain. Number of patients. 0, none; 1, moderate; 2, severe.

		Group S	Group M
Pain, 1 hour	0	6	13
	1	32	27
	2	12	10
Pain, 2 hours	0	13	17
	1	31	29
	2	6	4

severity of pain in the knee during the recovery period was almost identical in both groups (Table 5). However, while only five patients received parenteral analgesia (three in Group S and two in Group M), a higher proportion of patients in Group M were given oral analgesia (22% compared with 8%).

Questionnaire

Forty-seven patients returned completed questionnaires. Twenty-seven of these were in Group M and 20 in Group S. The number of patients who complained of moderate sleepiness on the first postoperative day was higher in Group S (60%) than in Group M (18.5%); (Table 6). There were no differences between groups in the incidences of headache or dizziness. One patient in each group complained of pain at the site of the injection on the first postoperative day. There was no significant difference in the number of analgesic tablets taken in each group.

Table 6. Incidence of sleepiness on first and second postoperative days, as assessed from questionnaires. 0, none; 1, moderate; 2, severe.

		Group S	Group M
Sleepiness Day 1	0	8 (40%)	20 (74.1%)
	1	12 (60%)	5 (18.5%)
	2	0	2 (7.4%)
Sleepiness Day 2	0	14 (70%)	22 (81.5%)
	1	5 (25%)	4 (14.8%)
	2	1 (5%)	1 (3.7%)

Thirteen patients (65%) in Group S and 21 patients (77%) in Group M felt that apart from pain or discomfort in the affected knee they would otherwise have been able to resume their normal activities on the first postoperative day. These numbers rose to 16 patients (80%) in Group S and 22 patients (81.5%) in Group M by the second postoperative day.

Discussion

This study confirms that the anaesthetic technique described, with or without midazolam pretreatment, is suitable for use in daycase surgery in that it provides smooth induction of anaesthesia, good recovery conditions and a low incidence of unpleasant side effects. The smooth induction conditions are of particular note in that despite the use of methohexitone, a drug known to cause pain on injection, hiccup and spontaneous muscle movement, none of these complications was noted in any of the 95 patients in the study who received the drug. The absence of pain on injection may be explained partly by the fact that the drugs were all given through a cannula placed in a large vein in the antecubital fossa. Premedication with opiate drugs is known to reduce the incidence of excitatory side effects of methohexitone and it is presumably the pretreatment with alfentanil which resulted in the complete absence of such complications in this study.

It is of note that the total anaesthetic time in Group S was significantly longer than that in Group M. The distribution of anaesthetic times was somewhat skewed by several longer surgical procedures, but nonparametric analysis of the times recorded still reveals significantly longer anaesthetic times overall in patients who received saline ($p < 0.05$). We postulate that the addition of midazolam resulted in a more rapid onset of anaesthesia of sufficient depth to allow the preparation of the patient for surgery (positioning on the operating table and the application and inflation of the tourniquet) and thus shortened the length of the procedure as a whole.

As expected, the addition of midazolam reduced by over 50% the dose of methohexitone needed to induce anaesthesia. However, despite this reduction and the longer anaesthetic time in Group S, the initial recovery from anaesthesia was prolonged in Group M. The time to awaken as defined by the time taken from the cessation of anaesthesia until the patient was able to give his or her full name correctly, was significantly longer in those patients who received midazolam (Table 1) and a smaller percentage of patients had awoken within 5 minutes and within 10 minutes than in the group which received saline. Furthermore the ability to perform the postbox and p-deletion tests was significantly worse in Group M at one hour postoperatively and these patients were almost twice as likely to complain of moderate sleepiness at this time. However, the incidence of sleepiness after 2 hours was almost the same in the two groups. Thus the addition of midazolam appears to have an adverse effect on initial recovery time although this effect is not apparent after 2 hours.

There was a low incidence of nausea in the study group as a whole (Table 4) and only four patients out of 100 required antiemetic therapy. The incidence of nausea was slightly higher in Group S, but the difference is not significant as the numbers affected were small. There was no evidence that the addition of midazolam reduced the degree of postoperative pain experienced by the patients in the study.

The poor response to the questionnaire, in that only 47% of the patients replied, makes it difficult to draw any firm conclusions about differences between the groups on the first and second postoperative days. However, amongst the patients who did reply, those in the saline group had a higher incidence of sleepiness on the first postoperative day.

This might result from their having received a larger dose of methohexitone. Overall, there appeared to be a low incidence of side effects attributable to the anaesthetic. Approximately 80% of the patients felt able to resume their normal activities by the second postoperative day.

In conclusion, it would seem that pretreatment with midazolam and alfentanil does not have any beneficial effects in comparison to the use of alfentanil alone in respect of the quality of recovery following daycase arthroscopy. The initial rate of recovery is slower despite the use of a smaller dose of induction agent. Furthermore, midazolam pretreatment does not lead to a significant reduction in postoperative pain.

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References

1. BEECHEY APG, ELTRINGHAM RJ, STUDD C. Temazepam as premedication in day surgery. *Anaesthesia* 1981; **36**: 10-5.
2. WHITE PF. Comparative evaluation of intravenous agents for rapid sequence induction—thiopental, ketamine, and midazolam. *Anesthesiology* 1982; **57**: 279-84.
3. VICKERS MD. The measurement of recovery from anaesthesia. *British Journal of Anaesthesia* 1965; **37**: 296-302.
4. CRAIG J, COOPER GM, SEAR JW. Recovery from day-case anaesthesia. Comparison between methohexitone, Althesin and etomidate. *British Journal of Anaesthesia* 1982; **54**: 447-50.
5. DIXON RA, THORNTON JA. Tests of recovery from anaesthesia and sedation: intravenous diazepam in dentistry. *British Journal of Anaesthesia* 1973; **45**: 207-15.

Suxamethonium dosage in electroconvulsive therapy

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Summary

A double-blind study was conducted in 52 patients who received a total of 180 electroconvulsive therapy treatments. Patients were allocated randomly to receive doses of 15 mg, 25 mg or 50 mg of suxamethonium. Those who received suxamethonium 50 mg took significantly longer to breathe again compared with patients who received the lower doses, and were significantly more likely to have a very well modified convulsion than patients who received suxamethonium 15 mg. There were no differences among the groups in the incidences of muscle pains after treatment. We conclude that all three doses were acceptable; however, a dose of 25 mg had practical advantages over 50 mg and theoretical advantages over 15 mg.

Key words

*Anaesthesia; electroconvulsive therapy.
Neuromuscular relaxants; suxamethonium.*

Suxamethonium has been used since 1951¹ to modify the muscular contractions associated with electroconvulsive therapy (ECT), but there seems to be little agreement about the optimum dose for this procedure or the degree of muscular relaxation required. An early paper suggested a dose of 75 mg to produce complete paralysis;² a technique that uses no muscle relaxants has been described,³ while standard textbooks advise doses of 25-40 mg or 0.5-0.75 mg/kg.⁴⁻⁵ In local practice, we use doses of 15-50 mg. The theoretical risk of using too low a dose of suxamethonium is that a violent convulsion may cause musculoskeletal injury to the patient whilst too high a dose may result in a patient who is awake but paralysed at the end of treatment.¹

The objective of our study was to compare suxamethonium doses of 15 mg, 25 mg and 50 mg in respect of the intensity of the grand mal convulsion, the incidence of post-therapy muscle pain and the time for adequate breathing to become re-established after treatment.

Methods

The study was approved by the local ethical committee, and informed consent was obtained from each patient, all of whom were under 80 years of age and weighed less than 100 kg. We excluded patients with whom we could not communicate, those who were receiving monoamine oxidase

inhibitors and patients with significant musculoskeletal disease. All patients were in ASA categories 1 or 2.

Thiopentone 250 mg was administered to male patients, and 200 mg to females, for induction of anaesthesia; increments of 100 mg were given if necessary until the patient became incapable of coherent speech. Suxamethonium was administered in a dose of 15, 25 or 50 mg, diluted to a volume of 1 ml. The dose was determined by random allocation, and the anaesthetist was unaware of the dose contained in the syringe. The lungs were ventilated with 100% oxygen via a Mapleson C system for one minute after the administration of suxamethonium. A tooth guard was then inserted. Following the convulsion, artificial ventilation of the lungs was continued until adequate spontaneous breathing returned.

Electroplexy technique

An electric stimulus was given from an Ectron Duopulse machine at the discretion of the psychiatrist between 60 and 75 seconds after the suxamethonium had been given. A second stimulus was applied if the first stimulus gave no response. No further stimuli were given if there was no response to that.

Observations

Observations were made by a consultant anaesthetist (W.K.) who was aided by a time keeper. Timing started

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when the suxamethonium was injected. The presence or absence of fasciculations, and the duration of the clonic phase of the grand mal seizure (whether over or under 15 seconds), were noted. The strength of the grand mal convulsion was graded as very well modified (little visible response or facial movement only); moderate (generalised movement of face and limbs but not torso); or vigorous (generalised movements of limbs and torso). The duration of apnoea was also recorded. All patients were interviewed before ECT by an experienced psychiatric nurse (W.B. or F.B.) and asked whether they had any troublesome aches or pains. Patients were interviewed again 24–48 hours after ECT to find out whether they had developed muscle pains or other symptoms. Patients who complained of pains before or after ECT were interviewed by an anaesthetist (W.K.) to determine the precise nature of these pains. Significance of differences was determined by Chi-square test or Student's *t*-test as appropriate.

Results

Fifty-two patients received 180 treatments and were grouped according to suxamethonium dosage. Group A received 15 mg, group B, 25 mg and group C, 50 mg. Data concerning age, weight, sex and medication of patients are shown in Tables 1 and 2. One patient in group B received one incre-

Table 1. Age, sex and weight of patients

	Group A	Group B	Group C
Dose (mg) of suxamethonium	15	25	50
Number of treatments	60	60	60
Male:female	20:40	28:32	22:38
Mean age, years (SD)	49.5 (18.3)	50.0 (17.4)	51.3 (16.6)
Mean weight, kg (SD)	63.4 (11.3)	65.8 (12.7)	67.2 (11.3)
Number of patients	32	34	30

Table 2. Drug therapy.

	Group A (15 mg) <i>n</i> = 60	Group B (25 mg) <i>n</i> = 60	Group C (50 mg) <i>n</i> = 60
Benzodiazepine	23	11	16
Non MAOI antidepressant	41	39	39
Lithium	8	17	17
Long acting antipsychotic	12	9	8
Butyrophenone or phenothiazine	18	28	23
Procyclidine	11	17	10
No drugs	2	2	3

ment of thiopentone 100 mg after the initial induction dose, and one patient in group C received two increments. Four patients had muscle pains which were related to treatment. A 35-year-old female (group A) who weighed 58 kg developed aching muscles across her chest, shoulders, thighs and buttocks. These resolved after 48 hours. A 52-year-old female (group A) who weighed 56 kg developed a pain in her masseters which lasted 3 days. A female aged 41 years (group B), and who weighed 66 kg, had neck pain and stiffness for 3 days after treatment. A female aged 75 years (group C) who weighed 47 kg had aching and stiffness of the calves and shoulders which lasted 7 days. All of

these patients received further ECT treatment without any problems. The musculoskeletal symptoms occurred after the first or second treatment. A number of patients complained of miscellaneous aches and pains, which included headache, discomfort after intramuscular injections, new trauma, old trauma and vague abdominal colic. These results are summarised in Table 3.

Table 3. Incidence of aches and pains.

	Group A	Group B	Group C
Pains before but not after treatment	5	2	3
Pains after treatment but not before	1	2	2
Pains before and after treatment	2	2	5
Muscle pains probably related to treatment	2	1	1

Fasciculations were noted after suxamethonium administration in 25 cases in group A, 27 cases in group B and 31 cases in group C. There were no significant differences among the groups. The mean time to recovery of adequate ventilation increased in proportion to the dose of suxamethonium given (Table 4). Patients who received suxa-

Table 4. Recovery of ventilation.

	Group A	Group B	Group C
Mean time to return of adequate ventilation after suxamethonium injection, minutes (SD)	3.8* (0.8)	4.2 (1.5)	5.2* (1.6)
Number who took more than 6 minutes to adequate ventilation	0	2	12**

* Significant difference between groups A and C; *p* < 0.01.

** Significant difference between group C and other two groups; *p* < 0.01.

methonium 50 mg were more likely to have apnoea of more than 6 minutes duration than patients who were given lower doses of suxamethonium. Patients with prolonged apnoea (> 6 minutes) in group C had a mean age of 66.6 years, a mean weight of 55.4 kg and a sex ratio of nine females to two males. The incidence of very well modified convulsions was significantly higher in group C than in group A. There were no other differences between groups in this respect (Table 5).

Table 5. Nature of grand mal convulsions.

	Group A <i>n</i> = 60	Group B <i>n</i> = 60	Group C <i>n</i> = 60
Very well modified	1*	3	8*
Moderate	48	45	46**
Vigorous	11	12	6*
Duration of fit less than 15 seconds	8	8	15**

* Significant difference between Groups A and C; *p* < 0.05.

** No significant difference between groups.

Discussion

The main influence of suxamethonium dose in this study related to the recovery of adequate ventilation after

ECT. The return of spontaneous breathing was delayed significantly in patients who received suxamethonium 50 mg, and these patients were significantly more likely to have a prolonged period of apnoea which lasted between 7 and 11 minutes. We were concerned that these patients might remember being awake and paralysed. However, the apnoeic patients tended to be small elderly females who, when interviewed later, had no recollection at all of their recovery period. It would appear that suxamethonium 50 mg is a satisfactory dose for most patients, but it may be desirable to give less to elderly patients who are light-weight.

There was also a difference between the incidences of very well modified convulsions in groups A and C. It might be inferred from this that suxamethonium 50 mg confers more protection against fractures than the lowest dose. However, there was no significant difference between the groups in the incidence of vigorous convulsions and patients who have vigorous convulsions may be more at risk of fractures than those who have moderate or very well modified convulsions. However, in order to put the problem of fractures after ECT into perspective, it should be remembered that such fractures are rare. There were six fractures in one series of 50 000 ECT treatments¹ given without any anaesthetic at all.

The debate about whether strong convulsions are more effective than heavily modified convulsions in the relief of depression is not yet resolved. Some psychiatrists believe that a healthy jerking of the limbs is therapeutic and request vigorous convulsions, whereas other psychiatrists are satisfied with a minimal physical response. Unfortunately, there are no published data to support either point of view. Consequently, it would seem reasonable to give patients low doses of suxamethonium if vigorous convulsions are required. The incidence of muscle pain after ECT was low in all groups, in agreement with previously reported findings,^{1,6} but the origin of the pains is not certain; they may arise from the convulsion or from the suxamethonium.

In one study, patients who received suxamethonium had significantly more muscle pains after ECT than patients who did not receive suxamethonium.³ Masseter pain is not uncommon after ECT and is a consequence of stimulation of the masseters by the ECT electrodes. Masseter spasm occurs in fully paralysed patients and should therefore probably not be related to the dose of suxamethonium used. From our survey of aches and pains after ECT we conclude that their incidence is unrelated to the dose of suxamethonium.

In conclusion, we consider that any of the three doses of suxamethonium which we studied is acceptable for ECT. There were no important differences between patients who received 15 mg and 25 mg. Patients who received 50 mg were more likely to have slow recovery of breathing and a very well modified fit. We consider that a dose of 15 mg or 25 mg is to be preferred.

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References

1. MCCLEAVE DJ, BLAKEMORE WB. Anaesthesia for electroconvulsive therapy. *Anaesthesia and Intensive Care* 1975; **3**: 250-6.
2. ADDERLEY DJ, HAMILTON M. Use of succinylcholine in ECT with particular reference to its effect on blood pressure. *British Medical Journal* 1953; **1**: 195-7.
3. DELILKAN AE. Electroconvulsive therapy no-relaxant anaesthesia. *British Journal of Anaesthesia* 1969; **41**: 884-9.
4. ATKINSON RS, RUSHMAN GB, ALFRED LEE J. *A synopsis of anaesthesia*, 9th edn. Bristol: John Wright and Sons, 1982: 433.
5. CHURCHILL-DAVIDSON HC. In: WYLIE WD, CHURCHILL-DAVIDSON HC, eds. *A practice of anaesthesia*, 5th edn. London: Lloyd-Luke Ltd, 1984: 790.
6. GOMEZ J. Subjective side-effects of ECT. *British Journal of Psychiatry* 1975; **127**: 609-11.

CASE REPORT

Isoflurane in the treatment of asthma

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Summary

A 22-month-old child developed severe bronchospasm. Prolonged ventilation of the lungs with isoflurane for 102 hours was used as treatment. The metabolism and fluoride levels obtained are discussed.

Key words

Anaesthetics, volatile; isoflurane.

Complications; asthma.

Asthma in children is a common disease. Phelan¹ suggests that 20% of children wheeze as a result of asthma at some stage of childhood, although in 60% of affected children the disease is trivial and in many cases medical advice is not sought. Children aged 3-7 years are most susceptible to wheezing problems but a significant number do present within the first 2 years of life and most of these episodes are associated with viral infections.¹ Standard medical management with beta adrenoceptor stimulants, methylxanthines and steroids controls most cases. This case history is of a patient who had an inadequate response to conventional management and who was treated with an inhalational agent.

Case history

A twenty-two-month-old girl was admitted with upper respiratory tract infection and difficulty in breathing, which had been preceded in the last 24 hours by loss of appetite and a dry cough. On admission she was afebrile, had laboured breathing with rib retraction and marked wheezing on auscultation. She had had multiple admissions with respiratory tract infections over the preceding year, and bronchospasm had been noted on these occasions. She also had spinal dysraphism which had caused her no problems.

Management consisted initially of oral aminophylline and salbutamol administered by nebuliser. There was marked deterioration in her condition in the next 24 hours despite administrations of intravenous aminophylline and hydrocortisone and she was transferred to the intensive care unit. She was clinically exhausted on arrival and in respiratory failure. Arterial blood gases at the time were pH 7.19,

PCO₂ 6.5 kPa, PO₂ 5.0 kPa breathing on a mask with an oxygen concentration of 50%. Tracheal intubation was effected with ketamine and suxamethonium in view of the severity of her presentation. Relaxation was continued with pancuronium and she was sedated by a pethidine infusion. Ventilation was extremely difficult with high airway pressures (5.5 kPa) despite trials with a variety of different ventilatory patterns. The aminophylline dose was increased and then changed to isoprenaline, but there was no resolution of the bronchospasm and the blood gases deteriorated; the PCO₂ increased to 8.8 kPa. At this time the core temperature was 38.8 °C and antibiotic treatment was started. The airway pressure was still very high, and the ventilation achieved inadequate, so adrenaline was administered by nebuliser. No improvement was noted so adrenaline was then given in high dosage intravenously.

The absence of a significant response to these measures left few alternatives, but three further manoeuvres were tried. Firstly, a large dose of methylprednisolone was given, secondly, the adrenaline infusion was changed to high-dose salbutamol and thirdly, an inhalation agent was commenced. A system was arranged so that isoflurane could be given in an air and oxygen mixture. The oxygen concentration and the isoflurane concentration were both measured proximal to the patient and isoflurane was commenced at 1.5%. There was an initial improvement and over the next few hours the airway pressure decreased to 3.5 kPa. However, there was evidence on chest X ray of interstitial emphysema and clinical surgical emphysema became apparent. A bronchoscopy was performed to clear any mucous plugs present and to exclude a foreign body as the cause of the bronchospasm. On the third day of

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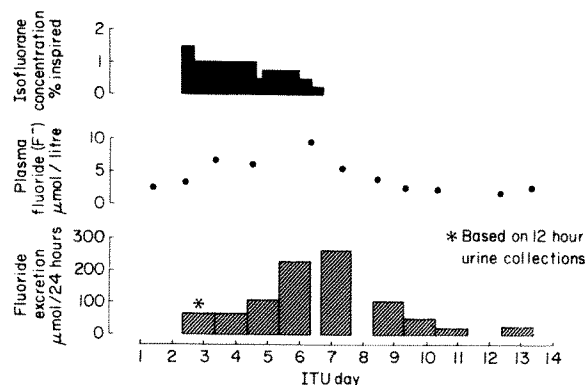


Fig. 1. Inspired concentration of isoflurane and measurements of both plasma and urine fluoride levels for the duration of the patient's stay on intensive care.

ventilation there was some minor improvement in the airway pressures and by the fourth day the airway pressure reduced markedly to the order of 2.7–3.0 kPa. The isoflurane was reduced during this time and a graph of the percentages is shown in Fig. 1. Eventually it was discontinued after 4 days of ventilation.

Ventilation at this stage was much improved but the oxygenation was still poor, presumably due to mucous plugs and resultant segmental collapse. Regrettably the child then had a large haematemesis. There was evidence on gastroscopy of stress ulceration which had occurred despite the use of H₂-antagonist prophylaxis and maintenance of persistently high gastric pH. The ulcer was oversewn.

The respiratory function improved over the next 7 days and she was weaned from the ventilator and discharged from intensive care. Results of viral studies taken following admission were all returned as negative.

A total of 73 MAC hours of isoflurane was used. Close monitoring of renal and hepatic function was performed during the course of this case. Additionally, fluoride levels in both plasma and urine were measured and the results are in Fig. 1.

The fluoride ion activity was determined in plasma and urine samples, with a fluoride ion-specific electrode (Orion Research Incorporated).² Plasma samples were considered suitable as the heparin anticoagulant contained negligible amounts of fluoride. Samples were diluted with a high ionic strength buffer before the estimation was performed to minimize interference by aluminium, iron and other cations. The difference between fluoride ion activity and fluoride ion concentration is minimal under these conditions.

Discussion

Patients in status asthmaticus may require controlled ventilation of the lungs in order to prevent hypoxia. Hypoxia is caused by increased breathing effort, less efficient ventilation associated with bronchospasm and widespread mucous plugging which results in increased ventilation/perfusion mismatch. In order to ventilate the patient sedation and paralysis are usually necessary. This may improve gas exchange and result in a decrease in peak airway pressure (in asthmatics) but have no direct

bronchodilator action.³ Inhalational anaesthetic agents, particularly ether and halothane, have been used as bronchodilators both in anaesthetic practice and in the management of severe asthmatics who have been unresponsive to other treatment. In this particular instance ether was contraindicated because of its flammability. The patient was in a cubicle, there was an abundance of electrical apparatus and no antistatic flooring. Halothane was also considered to be contra-indicated because of its dysrhythmogenic effect especially as (at the time of intubation) the patient had raised *Paco*₂ and was on sympathomimetic agents.⁴ The subsequent use of adrenaline would also have caused problems had halothane been used. Isoflurane was chosen because while it has a bronchodilator action, it is less dysrhythmogenic and also has a low rate of metabolism.

Both short⁵ and prolonged⁶ use of isoflurane as a bronchodilator in asthma have been described. However, while isoflurane and halothane have both been shown to be effective in diminishing allergic bronchoconstriction in the animal model⁷, Heneghan *et al.*⁸ could only demonstrate minimal bronchodilator action of isoflurane in healthy patients. Isoflurane did appear to be beneficial in this case.

The prolonged use of any inhalational agent raises the possibility of toxicity. Previous reports describe the prolonged use of isoflurane for other reasons, in adults for 6–11 hours⁹ and in a child for 25 MAC hours¹⁰ and also for 48 hours.¹¹ No organ toxicity was noted in any of these reports. In this case isoflurane was administered for 102 hours or an estimated 73 MAC hours, which is longer than previous reports. In view of this there was concern that metabolism of this agent might lead to toxicity. Metabolism of isoflurane and release of free fluoride has been studied by various authors.^{12–14} Free fluoride levels which exceed 50 μmol/litre are associated with defects in renal concentrating ability.¹⁵ However Mazze *et al.*¹⁶ suggest that the threshold for organic fluoride toxicity is lower than previously suspected. This may be because organ toxicity is related to both the peak level and the length of time the organ is exposed to the agent. In the case described here the peak inorganic fluoride level was 9.5 μmol/litre which was higher than those recorded in adults by Oikkonen.⁹ This difference may be because of the length of exposure to isoflurane or possibly because of a different mechanism of metabolism. Differences in metabolism have been noted with other anaesthetic agents^{17,18} and it has been suggested that these differences may be genetic. There may be an age-related difference in metabolism, although this seems unlikely. Alternatively the rise in fluoride concentration may demonstrate an effect suggested by Plummer *et al.*,¹⁴ that the metabolism of isoflurane is greater than initially anticipated because when used for short anaesthetics, rapid excretion of isoflurane from the lungs leaves little available for metabolism. Saturation occurs with prolonged use of isoflurane and therefore a larger quantity of it is available for metabolism.

The fluoride derived from metabolism of isoflurane is presumed to have a similar fate to fluoride that has been orally administered. Fluoride taken orally is absorbed freely and 40–50% of the dose is incorporated rapidly into bone as fluoro-apatite, the remainder is excreted in urine.¹⁹ The exposure of this patient to fluoride, as judged by the daily

urine excretion, was considerably in excess of that advised for children.²⁰ However, while chronic exposure to an excess of fluoride may cause the skeletal and dental changes of fluorosis there is no evidence that short term exposure, as in this case, has any long-term effect on skeletal or dental development.

No abnormality of renal function as monitored by volume, blood urea and creatinine was detected in this patient and the creatinine and urea clearance remained normal (Fig. 1). Therefore there is no clinical evidence that any nephrotoxicity occurred following the prolonged use of isoflurane. The serum levels of both alanine amino-transferase (ALT) and aspartate transaminase (AST) reached a peak on the same day as the organic fluoride peak occurred. These levels were elevated above the normal range, but both had returned to within normal the next day. There were a variety of other potential causes for a mild disturbance of the liver-function tests at this time so these data cannot be taken as evidence of hepatotoxicity. Plummer *et al.*¹⁴ found no significant differences in the body weight ratio, the serum ALT activities or liver pathology in rats after prolonged exposure to isoflurane as compared with controls.

References

1. PHELAN PD. Asthma in children. *Medicine International* 1987; **2**: 1526-30.
2. COWELL DC. The determination of fluoride ion concentration in biological fluids and in the serum and urine of fluoride-treated patients with Paget's disease and osteoporosis. *Medical Laboratory Technology* 1975; **32**: 73-89.
3. LEVIN N, DILLAN JB. Status asthmatics and pancuronium bromide. *Journal of the American Medical Association* 1972; **222**: 1265-8.
4. ROIZEN MF, STEVENS MC. Multifocal ventricular tachycardia due to the interaction of aminophylline and halothane. *Anesthesia and Analgesia Current Researches* 1978; **57**: 738-41.
5. PARNASS SM, FELD JM, CHAMBERLIN WH, SEGIL LJ. Status asthmatics treated with isoflurane and enflurane. *Anesthesia and Analgesia* 1987; **66**: 193-5.
6. BIERMAN MI, BROWN M, MUREN O, KEENAN RL, GLAUSER FL. Prolonged isoflurane anesthesia in status asthmatics. *Critical Care Medicine* 1986; **14**: 832-3.
7. HIRSHMAN CA, EDELSTEIN G, PEETZ S, WAYNE R, DOWNES H. Mechanism of action of inhalational anesthesia on airways. *Anesthesiology* 1982; **56**: 107-11.
8. HENEGHAN CPH, BERGMAN NA, JORDAN C, LEHANE JR, CATLEY DM. Effect of isoflurane on bronchomotor tone in man. *British Journal of Anaesthesia* 1986; **58**: 24-8.
9. OIKKONEN M. Isoflurane and enflurane in long anaesthesias for plastic microsurgery. *Acta Anaesthesiologica, Scandinavica* 1984; **28**: 412-8.
10. PEARSON J. Prolonged anesthesia with isoflurane. *Anesthesia and Analgesia* 1985; **64**: 92-3.
11. KOFKE WA, SNIDER MT, YOUNG RSK, RAMER JC. Prolonged low flow isoflurane anesthesia for status epilepticus. *Anesthesiology* 1985; **62**: 653-6.
12. MAZZE RI, COUSINS MJ, BARR GA. Renal effects and metabolism of isoflurane in man. *Anesthesiology* 1974; **40**: 536-42.
13. DOBKIN AB, DUCKSOOK K, CHOI JK, LEVY AA. Blood serum fluoride levels with enflurane and isoflurane anaesthesia during and following major abdominal surgery. *Canadian Anesthetists' Society Journal* 1973; **20**: 494-8.
14. PLUMMER JL, HALL P DE LA M, JENNER MA, ILSLEY AH, COUSINS MJ. Effects of chronic inhalation of halothane, enflurane or isoflurane in rats. *British Journal of Anaesthesia* 1986; **58**: 517-23.
15. COUSINS MJ, MAZZE RI. Methoxyflurane nephrotoxicity. A study of dose response in man. *Journal of the American Medical Association* 1973; **225**: 1611-6.
16. MAZZE RI, CALVERLEY RK, SMITH NT. Inorganic fluoride nephrotoxicity: prolonged enflurane and halothane anesthesia in volunteers. *Anesthesiology* 1976; **46**: 265-71.
17. HETRICK WD, WOLFSON B, GARCIA DA, SIKER ES. Renal responses to 'light' methoxyflurane anesthesia. *Anesthesiology* 1973; **38**: 30-7.
18. CASCORBI HF, VESELL ES, BLAKE DA, HELRICH M. Genetic and environmental influence on halothane metabolism in twins. *Clinical Pharmacology and Therapeutics* 1971; **12**: 50-5.
19. SPENCER H, LEWIN I, WISHROWSKI E, SAMACHSON J. Fluoride metabolism in man. *American Journal of Medicine* 1970; **49**: 807-813.
20. American Academy of Pediatrics. Committee on nutrition. Fluoride supplementation: revised dosage schedule. *Pediatrics* 1979; **63**: 150-2.

CASE REPORT

The nasocardiac reflex

M. L. BAXANDALL AND J. L. THORN

Summary

The oculocardiac reflex is well described and recognised in anaesthesia. The nasocardiac reflex is less well-known. We describe a clinical manifestation of this reflex and describe the relevant anatomy. This reflex may be obtunded during general anaesthesia.

Key words

Surgery; ear, nose and throat.

Complications; dysrhythmia.

The oculocardiac reflex is well described and recognised in anaesthesia.^{1,2} The nasocardiac reflex³ is less well-known. We present a manifestation of this reflex which occurred during a routine rhinological operation.

Case history

A 69-year-old male was admitted for intranasal antrostomies. The patient's history revealed respiratory difficulty caused by a nasal blockage but no other respiratory problem. He took regular exercise, had no symptoms of cardiac ischaemia, was taking no medication and admitted to no allergies. He had a direct laryngoscopy under local anaesthesia 2 months previously and a general anaesthetic in the past for haemorrhoidectomy. That anaesthetic passed without incident. On examination he was an obese man and weighed 92 kilograms with a pre-operative blood pressure of 170/100 mmHg. A pre-operative electrocardiogram revealed sinus rhythm with a rate of 65 beats/minute and no evidence of ischaemic heart disease. The PR interval was at the upper limit of normal at 0.2 second.

The patient was premedicated one hour pre-operatively orally with temazepam 30 mg. Blood pressure on arrival in the anaesthetic room was 170/100 mmHg as measured with a mercury sphygmomanometer. He was pre-oxygenated and anaesthesia induced with thiopentone 400 mg, fentanyl 100 µg and suxamethonium 100 mg. Tracheal intubation was performed and adequate ventilation of the lungs verified by auscultation. Anaesthesia was maintained with nitrous oxide 66%, oxygen 33% and isoflurane 1%. Muscular relaxation was maintained with atracurium 30 mg. The patient was connected to a noninvasive pressure monitor and electrocardiogram and the pulse was

monitored by digital plethysmometry. The surgeon introduced a nasal speculum into the right naris and the turbinate bones were manipulated. A profound bradycardia was noted immediately with only one complex seen on the electrocardiogram monitor for two complete sweeps (8 seconds duration). The surgeon was asked to stop operating and the inspired oxygen concentration increased to 100%. Atropine 0.5 mg was given intravenously and normal saline 500 ml was infused rapidly. The electrocardiogram indicated sinus rhythm with a rate of 65 beats/minute, 2 minutes after the administration of atropine, and over the next 10 minutes the blood pressure was restored to 100 mmHg systolic having previously been unrecordable. Nitrous oxide and isoflurane were re-introduced at this stage and, having given atropine intravenously, it was considered safe to continue. However, as soon as the nasal speculum was re-introduced into the nose and the inferior turbinates were touched with forceps a further profound bradycardia was precipitated once more. The instruments were removed from the nose and sinus rhythm returned, this time without associated hypotension. The procedure was abandoned and the patient allowed to breathe spontaneously when the atracurium had worn off, thus the use of cholinergic drugs was avoided. The patient was transferred postoperatively to the intensive care unit for 12 hours during which time his blood pressure and pulse were stable at the pre-operative levels. Serial electrocardiograms and cardiac enzymes did not suggest myocardial infarct. The patient made a full recovery.

Anatomy

The nerve supply to the nose can be divided into that to

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the lateral wall and that to the nasal septum.⁴ If the lateral wall is bisected by a vertical and horizontal line each quadrant receives a separate supply.

The posterosuperior quadrant. This is supplied by the posterior superior lateral nerves from the pterygopalatine ganglion.

The postero-inferior quadrant. This is supplied by the anterior palatine nerve, which pierces the perpendicular plate of the palatine bone and passes forwards into the nasal mucous membrane.

The anterior-superior quadrant. This is supplied by the anterior ethmoidal nerve which passes down through the nasal slit in the cribriform plate. The nerve gives off lateral branches and medial branches and passes out of the surface between the nasal bone and upper nasal cartilage, where it is called the external nasal nerve.

The anteriorinferior quadrant. This is supplied by the anterior superior alveolar nerve.

The nerve supply of the septum is as follows. The nasopalatine nerve enters the sphenopalatine foramen and passes medially across the roof of the nose to the upper part of the posterior border of the septum and supplies the postero-inferior part of the septum. The anterosuperior part of the septum is innervated by the septal branches of the anterior ethmoidal nerve.

The sensory nerve supply of the nose arises from the maxillary branch of the trigeminal nerve. Sympathetic and parasympathetic (vagal) fibres enter the sphenopalatine ganglion from the deep petrosal nerve. Thus every branch from the sphenopalatine ganglion carries a mixture of three kinds of fibres: sensory, secretomotor (parasympathetic) and sympathetic. The afferent stimulus of the nasocardiac reflex travels in the maxillary division of the

trigeminal nerve, and the efferent pathway to the heart is via the vagus nerve.

Discussion

The anatomy of the nerve supply to the nose is outlined above. The patient we describe had a very pronounced nasocardiac reflex and if surgery was contemplated in this region again the reflex would have to be obtunded either by pharmacological methods, such as a parasympathetic blockade with atropine, or with local anaesthesia. The insertion of a temporary transvenous cardiac pacing wire should also be considered. We believe that this case also emphasises the need for adequate monitoring of all patients who undergo anaesthesia regardless of how trivial the surgery may be.

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References

1. DEWAR KMS, WISHART HY. The oculocardiac reflex. *Proceedings of the Royal Society of Medicine* 1976; **69**: 373-4.
2. ADAMS AK, JONES RM. Anaesthesia for eye surgery: general considerations. *British Journal of Anaesthesia* 1980; **52**: 663-9.
3. SLOME D. Physiology of the nose and paranasal sinuses. Reflexes initiated from the nose. In: BALLANTYNE J, GROVES J. eds. *Scott-Brown's Diseases of the ear, nose and throat. Vol I. Basic sciences*, 3rd edn. London: Butterworths, 1971; 169-73.
4. LAST RJ. *Anatomy: regional and applied*. Edinburgh: Churchill Livingstone, 1984: 403.

CASE REPORT

Anaesthetic management in patients with epidermolysis bullosa dystrophica

R. HAGEN AND C. LANGENBERG

Summary

Successful anaesthetic management of two patients with severe epidermolysis bullosa dystrophica was accomplished with the use of ketamine-diazepam dissociative anaesthesia in one and brachial plexus block in the other. The classification and pathology of epidermolysis bullosa is considered, and the problems associated with anaesthesia in patients with this disease are discussed.

Key words

Anaesthetics, intravenous; ketamine.
Anaesthetic techniques, regional; brachial plexus.

Epidermolysis bullosa (EB) is a mechanobullous disorder of the skin and mucous membranes which presents considerable problems for the anaesthetist. Tracheal intubation may provoke severe complications within the upper airway, the attachment of anaesthetic or monitoring apparatus is liable to produce lesions and general debility is a common feature of the disease. EB is one of a group of skin diseases in which increased collagenase activity is the fundamental

abnormality. This leads to collagen degeneration which results in splitting of the various epidermal layers, or at the transition between epidermis and dermis.^{1,2} The different types of EB (Table 1) are distinguished by the site at which splitting occurs and whether or not healing produces scar formation³.

Epidermolysis bullosa dystrophica (EBD), described first by Fox in 1879,⁴ is an autosomal recessive disorder with an

Table 1. Classification of types of epidermolysis bullosa (EB).

Disorder	Characteristics
I <i>Nonscarring EB</i>	
a. EB simplex, generalised	Autosomal dominant. Begins at birth or very early in life. Generalised blister formation, especially at pressure sites. Oral blisters rare. Aggravated by warm weather. Nails and teeth normal. Mildly to moderately incapacitating.
Pathology:	Intra-epidermal blister formation as the result of cytolysis of the basal membrane.
b. EB simplex, localised	Autosomal dominant. Blisters occur exclusively on limbs. Mildly to moderately incapacitating.
Pathology:	As in Ia.
c. EB junctional form	Autosomal recessive. Begins at birth. Generalised blister formation. Often lesions around mouth. Sometimes tracheal lesions. Severe anaemia and retarded growth. Death usually occurs before the 2nd year of life.
Pathology:	Subepidermal blister formation with splitting occurring immediately above the basal membrane.
II <i>Scarring EB</i>	
a. EB dystrophica, dominant	Autosomal dominant. Begins in childhood. Particularly affects limbs. Oral lesions rare. Teeth and nails normal. Hypertrophic scars often occur on healing. Moderately incapacitating.
Pathology:	Subepidermal blister formation. Splitting occurs immediately below basal membrane. Reduction in, or total absence of, anchor fibrils.
b. EB dystrophica, recessive	Autosomal recessive. Begins at birth or in early childhood. Severe, generalised blister formation. Atrophic scars are frequent after healing. Fusion of fingers common. Nails absent. Teeth dysplastic. Usually severe lesions of oesophagus and oropharynx. Anaemia. Severely incapacitating. Death usually occurs before the 30th year of life.
Pathology:	As in IIa.
c. Acquired EB	No evidence of heredity. Begins in adult life. Blisters do not become inflamed and remain localised. Oral lesions very fleeting. Underlying disease should be excluded.
Pathology:	Subepidermal blister formation. Splitting immediately below basal membrane. Amorphous matter beneath the basal lamina.

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incidence of 1:300 000 births⁵. Abnormalities are detected soon after birth or in early childhood. Bullae and erosions of the skin and mucous membranes appear after the slightest trauma, and often become secondarily infected and haemorrhagic. Hypergranulation often develops as the lesions heal, and scar retraction produces severe deformities such as flexion contractures and pseudosyndactyly. Abnormalities of the hair, nails and teeth are also associated with the disease^{5,6}. Lesions in the oropharynx produce gross adhesions such as cleavage of the tongue to the palate or floor of the mouth and often reduce the extent to which the mouth can be opened (microstomia).^{7,8} Oesophageal lesions lead to the formation of webs and strictures which may limit the intake of food. The combination of inadequate nourishment and the constant loss of fluid, protein and blood from the various lesions, results in malnutrition, dehydration, electrolyte disturbances, hypoproteinaemia and anaemia. Porphyria, renal insufficiency and amyloidosis are frequent accompaniments of EBD^{5,6}. The majority of patients die before their 30th year.

Treatment consists of the administration of corticosteroids systemically to limit the extent of scar formation, phenytoin to reduce collagenase activity or synthesis^{2,9,10} and local treatment. Prevention of trauma is of the utmost importance. Anaesthesia may be required for dental extractions, removal of scar tissue, relief of oesophageal strictures and correction of pseudosyndactyly. These patients may also require an anaesthetic for unrelated conditions.^{11,12}

Case histories

Case 1

Patient A was a 45-year-old man who had been diagnosed as suffering from EBD at the age of 3 months. He had a history of numerous operations for oesophageal stricture (webbing with hypergranulation), and for webbing of the fingers (pseudosyndactyly). He had also had all his teeth extracted. In addition, this patient had been admitted to hospital on many occasions for treatment of iron and folic acid deficiency anaemia and hypoproteinaemia. Body weight on admission was 60 kg and his height was 175 cm. Surgery was required for the removal of hypergranulating, haemorrhagic lesions of the buttocks. Erosions were present on the medial side of the forearms, between the knees, on the ankles and the soles of the feet, and around the mouth and nose. There were also flexion contractures of the fingers of both hands.

The patient had been treated with corticosteroids in the past but at the time of admission he was taking phenytoin 100 mg t.i.d. and was applying trichloroacetic acid 3% in carbowax to his lesions. Pre-operative investigations (Table 2) revealed an iron deficiency anaemia, thrombocytosis, mild electrolyte and renal function disturbances, and hypoproteinaemia. Blood transfusion raised the haemoglobin concentration to 5.9 mmol/litre before surgery. The patient was premedicated with atropine sulphate 0.5 mg intramuscularly. The operating table was covered with damp, warmed towels, under which was placed a thick layer of wadding. Monitoring consisted of pulse plethysmography, capnography and blood pressure recordings, and needle electrodes were used to record the electrocardiogram (ECG). Peripheral blood perfusion was recorded

Table 2. Results of pre-operative haematological and biochemical investigations in Patient A.

Investigation	Value	Normal range
Haemoglobin (mmol/litre)	2.9	8.6-10.9
Mean corpuscular volume (flitre)	78	83-104
Mean corpuscular haemoglobin (fmol)	1.5	1.7-2.2
Mean corpuscular haemoglobin concentration (mmol/litre)	18	19-23
Platelets ($\times 10^9$ /litre)	599	150-350
Sodium (mmol/litre)	146	136-146
Potassium (mmol/litre)	5.2	3.8-5.0
Chloride (mmol/litre)	110	99-108
Urea (mmol/litre)	9.2	3.0-7.5
Creatinine (μ mol/litre)	148	50-120
Total protein (g/litre)	59	62-78
—albumin (%)	25	60-72
Serum iron (μ mol/litre)	3	14-32
Iron binding capacity (μ mol/litre)	29	24-55
Iron saturation	0.09	0.25-0.60

from an earlobe and the blood pressure from the left arm using a padded cuff. An infusion was set up in the right internal jugular vein and secured with paper adhesive tape to the hair. Anaesthesia was induced in the right lateral position with ketamine 100 mg intravenously. A mixture of N₂O/O₂, 70/30% was delivered at a flow rate of 6 litres/minute via a mask using a circle system. The mask was covered with wadding and the skin with which it came into contact was smeared with 0.5% corticosteroid ointment. The patient breathed spontaneously, and nitrous oxide was supplemented with diazepam 5 mg and increments of ketamine to a total of 275 mg. The procedure lasted one hour, after which the patient woke up in the recovery room and was able to respond to commands. No new lesions appeared in the first 24 hours after operation. There were no psychomimetic effects from ketamine.

Case 2

Patient B was a man aged 26 years with a weight of 53 kg and a height of 178 cm. EBD had been diagnosed at birth. The patient had previously undergone repeated operations for webbing of the fingers of both hands.

On admission his body was covered with fresh bullae and large areas of eroded skin, with scattered hypergranulation tissue. Pre-operative investigations (Table 3)

Table 3. Results of pre-operative haematological and biochemical investigations in Patient B. Normal ranges are shown in Table 2.

Investigation	Result
Haemoglobin (mmol/litre)	5.5
Mean corpuscular volume (flitre)	64
Mean corpuscular haemoglobin (fmol)	1.2
Mean corpuscular haemoglobin concentration (mmol/litre)	18.8
Sodium (mmol/litre)	139
Potassium (mmol/litre)	4.2
Chloride (mmol/litre)	102
Urea (mmol/litre)	2.7
Creatinine (μ mol/litre)	55
Total protein (g/litre)	71
—albumin (%)	36
Serum iron (μ mol/litre)	5
Iron binding capacity (μ mol/litre)	45
Iron saturation	0.10

showed an iron deficiency anaemia and hypoalbuminemia, and he had multiple vitamin deficiencies (A, B₆, C, E and carotene). Further surgery for webbing of the fingers of the right hand was required together with the application of a Thiersch graft (Fig. 1). The patient was premedicated with



Fig. 1. Patient B. Pseudosyndactyly.

temazepam 20 mg by mouth. The monitors were attached in the operating room. The blood pressure cuff was padded and the ECG needle electrodes were secured by means of a circumferential elastic bandage.

Anaesthesia consisted of an interscalene brachial plexus block, with mepivacaine 2% 27 ml. The brachial plexus was located with a nerve stimulator. Motor block and complete analgesia were accomplished from C₅ to T₁. Although this patient had bullae at the site of puncture for regional block, there was no deterioration, and no new lesions developed postoperatively.

This patient required anaesthesia 8 months later for the same procedure on the left hand. His left brachial plexus was blocked as described above with mepivacaine 2% 30 ml. Once again there were no new lesions at the site of puncture.

Discussion

Patients with epidermolysis bullosa dystrophica require very special attention both before and during anaesthesia. Anaemia, hypoproteinaemia and electrolyte imbalance frequently demand pre-operative correction. Parenteral feeding may be necessary in cases of severe malnutrition.^{6,13} The extent of the lesions (e.g. bullae, scar formation, oropharyngeal strictures) must be ascertained carefully and recorded in advance. Premedication should not be administered subcutaneously or intramuscularly because of the danger of bulla formation at the puncture site.

The choice of anaesthetic technique and the extent of peri-operative monitoring depend upon the operation to be performed, the extent of the lesions and the general condition of the patient. Skin lesions, particularly those which result from friction^{11,12,14,15} can and must be avoided. It is preferable to let the patient place himself on the operating table in the position required for the operation.¹² The table must have a smooth surface and be well padded with

wadding.¹¹ Apparatus to monitor the patient must be attached without provoking trauma. Adhesive materials must not be used, and therefore ECG needle electrodes are preferred. Similarly, intravenous and intra-arterial catheters should be secured by means of elastic bandages or sutures. It is often necessary to insert a central venous catheter. Indirect blood pressure measurement requires an adequately padded cuff.

Hydrocortisone ointment 0.5% should be applied prophylactically at all sites where pressure or friction are liable to occur, e.g. knees, heels, elbows. These areas must be well padded. Potential difficulties with tracheal intubation should be assessed carefully. Microstomia, strictures or webbing of the oropharynx can make intubation impossible.

Bullae can develop within minutes at sites covered with pavement epithelium as the result of manipulations of the tracheal tube.^{7,15,16,21} However, as bullae do not form where ciliated epithelium is present, the tracheal mucosa is unaffected.^{8,11,16,17} Consequently, a tracheostomy should not cause major problems. Liberal application of lubricant jelly to the tracheal tube and laryngoscope blade is advised.^{8,14,17-19} Depolarising muscle relaxants must be avoided because of the muscle twitching they produce, as well as excessive release of potassium in the presence of muscle atrophy.¹⁵ Nondepolarising muscle relaxants are unpredictable in their duration because of the reduction in muscle tissue and the decrease in protein binding (hypoalbuminaemia). In addition, recurarisation can have disastrous consequences if emergency re-intubation is required. Atracurium may be the nondepolarising relaxant of choice because it is not excreted either by the liver or the kidneys, which may be affected by amyloidosis.²⁰

Patients who suffer from EBD are more liable to have porphyria, and barbiturates must be avoided. Morphine is contraindicated as an analgesic because it releases histamine. One method of avoiding all the difficulties described above is to use ketamine dissociative anaesthesia.^{12,21-23} Hypnosis and analgesia are provided, the swallowing and cough reflexes are maintained and tracheal intubation is not required.²⁴ However, ketamine is contraindicated in the presence of hypertension, myocardial insufficiency, psychiatric disorders and raised intracranial pressure.^{24,25} The psychomimetic side effects can usually be prevented by the administration of benzodiazepines. Intubation of the trachea can also be avoided by manual inflation of the lungs via a mask. Sites of pressure from the mask must be pretreated with hydrocortisone ointment.^{12,14-17,19,26,27}

Consideration should be given to methods of regional analgesia in order to avoid all contact with the oropharynx.^{21,28} The skin must be very carefully disinfected by pouring the solution over the skin, but any form of rubbing must be avoided. Local infiltration of the skin must not be performed. It is our opinion that, contrary to statements in the literature,^{11,12} uninfected bullae at the puncture site are not a contraindication to regional techniques. Local or regional techniques are not applicable if the nature of the operation renders them unsuitable, coagulation disturbances exist, the intended puncture site is infected or the patient is unsuitable for the method or refuses it.

Ketamine dissociative anaesthesia was chosen for our first patient because infected bullae in the lumbar region prohibited the use of a regional block, while microstomia

and cleavage of the tongue to the palate made tracheal intubation inadvisable.

Brachial plexus block was carried out on two occasions on the second patient because the bullae at the injection site were not infected. No new bullae developed at this site postoperatively.

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References

1. PEARSON RW. Studies on the pathogenesis of epidermolysis bullosa. *Journal of Investigative Dermatology* 1962; **39**: 551-75.
2. BAUER EA, GEDDE-DAHL T JR, EISEN AZ. The role of human skin collagenase in epidermolysis bullosa. *Journal of Investigative Dermatology* 1977; **68**: 119-24.
3. PEARSON RW. The mechanobullous diseases (epidermolysis bullosa). In: FITZPATRICK TB, ed. *Dermatology in general medicine*. New York: McGraw-Hill, 1971: 621-43.
4. FOX T. Notes on unusual or rare forms of skin disease. IV Congenital ulceration of the skin (two cases) with pemphigus eruption and arrest of development generally. *Lancet* 1879; **1**: 766-7.
5. ROOK A, WILKINSON DS, EBLING FJG. *Textbook of Dermatology*, 3rd edn. Oxford: Blackwell Scientific Publications, 1979.
6. SMITH GB, SHRIBMAN AJ. Anaesthesia and severe skin disease. *Anaesthesia* 1984; **39**: 443-55.
7. PRATILAS V, BIEZUNSKI A. Epidermolysis bullosa manifested and treated during anesthesia. *Anesthesiology* 1975; **43**: 581-3.
8. JAMES IG. Epidermolysis bullosa dystrophica. *Anaesthesia* 1983; **38**: 1106.
9. BAUER EA, COOPER TW, TUCKER D, ESTERLY NB. Phenytoin therapy of recessive dystrophic epidermolysis bullosa. Clinical trial and proposed mechanism of action on collagenase. *New England Journal of Medicine* 1980; **303**: 776-81.
10. BAUER EA, COOPER TW. Therapeutic considerations in recessive dystrophic epidermolysis bullosa. *Archives of Dermatology* 1981; **117**: 529-30.
11. MILNE B, ROSALES JK. Anaesthesia for correction of oesophageal stricture in a patient with recessive epidermolysis bullosa dystrophica: case report. *Canadian Anaesthetists' Society Journal* 1980; **27**: 169-71.
12. REDDY ARR, WONG DHW. Epidermolysis bullosa. A review of anaesthetic problems and case reports. *Canadian Anaesthetists' Society Journal* 1972; **19**: 536-48.
13. LEE C, NAGEL EL. Anesthetic management of a patient with recessive epidermolysis bullosa dystrophica. *Anesthesiology* 1975; **43**: 122-4.
14. YOUNG DA, HARDWICK PB. Anaesthesia for epidermolysis bullosa dystrophica. *Anaesthesia* 1968; **23**: 264-7.
15. ZACKHEIM HS, RUDZINSKY OJ, KATZ J, SPADEMAN RG. Skin and bone disorders In: KATZ J, KADISH B, eds. *Anesthesia and uncommon diseases*. Philadelphia: W.B. Saunders, 1973; 445-7.
16. BERRYHILL RE, BENUMOF JL, SAIDMAN LJ, SMITH PC, PLUMER MH. Anesthetic management of emergency cesarean section in a patient with epidermolysis bullosa dystrophica polydysplastica. *Anesthesia and Analgesia* 1978; **57**: 281-3.
17. FROST PM. Epidermolysis bullosa dystrophica. *Anaesthesia* 1981; **36**: 79.
18. TOMLINSON AA. Recessive dystrophic epidermolysis bullosa: the anaesthetic management of a case for major surgery. *Anaesthesia* 1983; **38**: 485-91.
19. JAMES I, WARK H. Airway management during anesthesia in patients with epidermolysis bullosa dystrophica. *Anesthesiology* 1982; **56**: 323-6.
20. WELCH DB. Anaesthesia and amyloidosis. *Anaesthesia* 1982; **37**: 63-6.
21. LOVERME SR, OROPOLLO AT. Ketamine anesthesia in dermolytic bullous dermatosis (epidermolysis bullosa). *Anesthesia and Analgesia* 1977; **56**: 398-401.
22. HAMANN RA, COHEN PJ. Anesthetic management of a patient with epidermolysis bullosa dystrophica. *Anesthesiology* 1971; **34**: 389-91.
23. KELLY AJ. Epidermolysis bullosa dystrophica—anaesthetic management. *Anesthesiology* 1971; **35**: 659.
24. SPOEREL WE, KANDEL PF. Clinical experiences with Ketalar. *Canadian Anaesthetists' Society Journal* 1971; **18**: 319-27.
25. SPIELMAN FJ, MANN ES. Subarachnoid and epidural anaesthesia for patients with epidermolysis bullosa. *Canadian Anaesthetists' Society Journal* 1984; **31**: 549-51.
26. MARSHALL BE. A comment on epidermolysis bullosa and its anaesthetic management for dental operations. A case report. *British Journal of Anaesthesia* 1963; **35**: 724-7.
27. PETTY WC, GUNTHER RC. Anesthesia for nonfacial surgery in polydysplastic epidermolysis bullosa (dystrophic). *Anesthesia and Analgesia* 1970; **49**: 246-50.
28. ROWLINGSON JC, ROSENBLUM SM. Successful regional anesthesia in a patient with epidermolysis bullosa. *Regional Anesthesia* 1983; **8**: 81-3.

CASE REPORT

Acute localised pulmonary oedema

Re-expansion pulmonary oedema following the surgical repair of a ruptured hemidiaphragm

S. T. KHOO AND F. G. CHEN

Summary

Re-expansion pulmonary oedema is a rare complication to follow the treatment of pneumothorax or pleural effusion. A unique case is described here which occurred in a young man immediately after the surgical repair of a ruptured diaphragm. The possible causative mechanisms are discussed.

Key words

Pulmonary oedema; localised.

Foucart (1875) and Ortnier (1899) were the first to describe pulmonary oedema as a complication of drainage of hydrothoraces. Subsequently, others reported a similar complication after the treatment of pneumothoraces.^{1,2} Acute unilateral pulmonary oedema was also described in a case which occurred in the operating room at the end of thoracotomy and pleurodesis for recurrent pneumothorax from a lung cyst.³ Our case is the first report in the literature of localised pulmonary oedema which developed immediately after the surgical repair of a ruptured hemidiaphragm.

Case history

A 23-year-old man was admitted to hospital after a road traffic accident. He had multiple bilateral rib fractures with a right haemothorax, and a traumatic rupture of the right hemidiaphragm with herniation of the liver into the pleural cavity which resulted in right lung collapse (Fig. 1). He also sustained fractures of the 12th thoracic, 1st, 4th and 5th lumbar vertebrae, which were associated with paraplegia. There was no evidence of head injury.

He was resuscitated successfully and the haemothorax was evacuated by a right thoracostomy. Six days later he was transferred to our hospital for thoracotomy and repair of the ruptured right hemidiaphragm; these procedures were performed 14 days after the injury. The right lung during the operation was found to be about 60% compressed by the liver and transverse colon, and required manual re-inflation with positive pressure ventilation after the surgical repair of the ruptured diaphragm. The lung looked normal after complete re-expansion with no evidence of contusion. An underwater seal chest drain was

inserted postoperatively and was allowed to drain passively.

The patient's lungs were ventilated electively in the intensive care unit after the operation. His condition deteriorated suddenly less than one hour after operation. He became sweaty, restless, tachypnoeic and hypotensive, and copious amounts of slightly blood-stained frothy sputum were aspirated from the trachea. A chest X ray (Fig. 2) showed pulmonary oedema in the right lower and middle lobes. Blood gas analysis showed a pH of 7.2, arterial carbon dioxide tension of 8.3 kPa and arterial oxygen tension of 6.5 kPa with an inspired oxygen concentration of 60%. Ventilation improved with positive end-expiratory pressure (PEEP) of +1 kPa and muscle paralysis. Central venous pressure was 10 cmH₂O.

Fluids were transfused and inotropic support started. The oedema fluid from the tracheal tube immediately turned yellow, the colour of the infusate when 20% albumin was given. Unfortunately no specimen was obtained for protein analysis. Eight hours later his condition improved markedly; a repeat chest X ray (Fig. 3) showed complete resolution of the pulmonary oedema. He continued to make good progress and was subsequently discharged to the general ward and thence to a rehabilitation unit.

Discussion

Pulmonary oedema is an abnormal collection of fluid in the extravascular tissues and spaces of the lung.⁴ Fluid exchange across the alveolar capillary membrane depends on both the hydrostatic and osmotic pressures of the intravascular and interstitial spaces. There is usually a net flow out of the intravascular compartment of fluid which is

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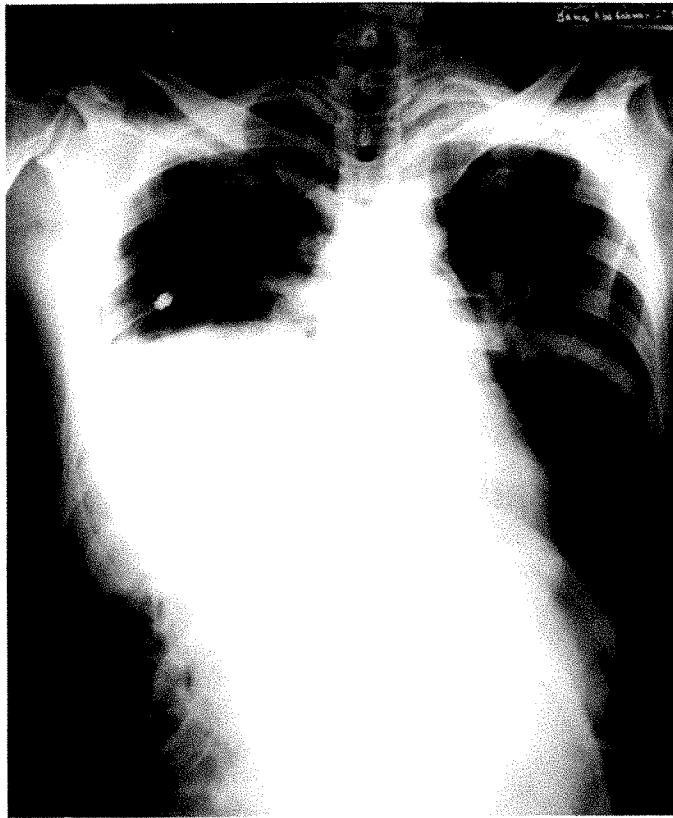


Fig. 1. Right haemothorax with herniation of liver and gut into the right pleural cavity from a ruptured hemidiaphragm. A chest tube had been inserted.

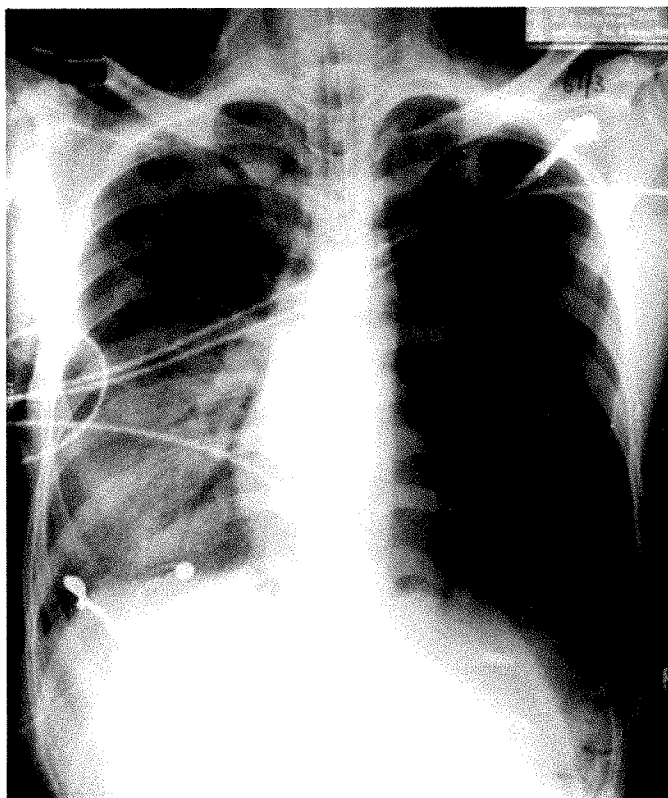


Fig. 2. Localised pulmonary oedema one hour after surgical repair of the ruptured right hemidiaphragm and manual re-expansion of the collapsed right lung.

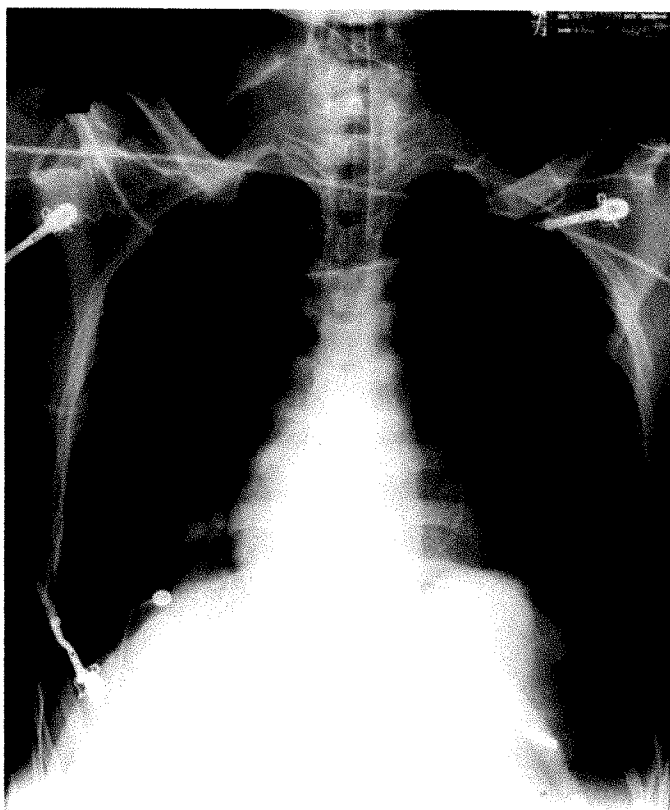


Fig. 3. A chest radiograph taken 8 hours after surgery.

returned to the systemic circulation via the lymphatics. Pulmonary oedema results when this flow is so excessive that the lymphatics are overwhelmed. This may be due to increases in capillary hydrostatic pressure or permeability. A comparison between the osmotic pressures or protein content of blood and oedema fluid can help to differentiate between these causes.^{5,6} Patients with cardiogenic or high pressure oedema tend to have a low oedema fluid:plasma protein ratio (0.46) whereas those with increased capillary permeability oedema have a higher ratio (0.6).⁷

Pulmonary oedema is traditionally bilateral whatever the cause. Re-expansion pulmonary oedema is unique in that it is localised and occurs when a previously collapsed lung or area of lung is rapidly re-inflated, for example during the treatment of pneumothorax or hydrothorax.⁸⁻¹⁰ A variety of factors are associated with its development. The duration and severity of the collapse are significant. In one case, pulmonary oedema was reported when re-expansion occurred after the lung had been collapsed for 3-7 days, but not when treatment was instituted within one day.¹¹ Animal studies also support this observation.¹² Re-inflation of the right lung in our patient was undertaken after 14 days of collapse and he promptly developed acute severe unilateral pulmonary oedema in the area of re-expansion. The speed at which the re-expansion is performed is also important. Application of a large negative pressure to intercostal drains to hasten the resolution of a pneumothorax has been implicated in a few cases.^{13,14} Re-expansion pulmonary oedema usually occurs early (within 3 hours) during the re-inflation and although some patients may be asymptomatic,⁸ the majority have symptoms that

range from slight cough to severe respiratory distress.^{1,2,3,5}

The consistent presence of a high protein content in the oedema fluid proves that re-expansion pulmonary oedema is caused by an increase in capillary permeability.^{6,15} Possible mechanisms include anoxic damage to the capillary endothelium secondary to prolonged collapse of the lung and mechanical damage to the blood vessel from overstretching during the process of re-expansion. Experimental studies in dogs have documented the presence of capillary disintegration with hyaline membrane formation when the lung is collapsed by bronchial ligation.¹⁶ This result, unfortunately, is not readily reproducible.¹⁷ Since there has been no demonstrable increase in permeability in the collapsed lung prior to re-inflation, it is possible that the process of re-expansion may damage the capillaries by mechanical overstretching.¹⁸ Application of excessive negative pressures to the intrapleural space to hasten the re-expansion may produce great pressure changes across the alveolar capillary membrane with resultant transudation into the alveoli.¹³ Bronchial obstruction is said to be an important prerequisite because a rapid influx of air into the alveoli would prevent development of a pressure gradient across the alveolar capillary membrane.¹⁹ However, not only has re-expansion pulmonary oedema been reported in patients with no evidence of bronchial obstruction,^{9,13} but it has also been noted after the collapsed lung has been re-inflated by positive pressure ventilation.^{3,14} It is tempting to implicate a decrease in surfactant activity as an aetiological factor. An increase in alveolar surface tension would tend to draw fluid into the

alveoli as well as impede re-inflation. When the lung is re-expanded forcefully, either by the application of an excessive negative intrapleural pressure or the use of positive pressure ventilation, mechanical injury to the pulmonary capillaries may result. Animal studies show that surfactant activity is normal in the re-expanded lung although the actual physical state of the surfactant in the collapsed lung is largely unknown.²⁰

It has been recommended that a lung that has been collapsed for more than three days should be re-expanded gradually.²¹ For example, the volume of fluid to be removed from a hydrothorax should not exceed 1.5 litres at any one time.¹⁰ Air should be removed slowly using an underwater seal drain, or if negative pressure is required, this should not exceed 2 kPa. Intermittent clamping of the chest tube may be necessary to reduce the speed of re-expansion. There is no great urgency to re-inflate a collapsed lung except in the presence of a tension pneumothorax. The intentional re-introduction of 50–100 ml of air to re-collapse the lung is said to be helpful in the prevention of severe pulmonary oedema.⁸

Our patient had several of the risk factors discussed above. Surgery was performed 14 days after the accident. The severely collapsed right lung was re-inflated with positive pressure ventilation, and controlled ventilation was continued in the intensive care ward. He developed severe localised pulmonary oedema within one hour after operation although no negative pressure was applied to the chest drain.

References

1. POULIAS GE, PROMBONAS E. Massive unilateral pulmonary oedema as a rapid re-expansion sequel (the post-expansion syndrome). Report of a case and review of the literature. *Scandinavian Journal of Thoracic and Cardiovascular Surgery* 1974; **8**: 67–9.
2. PEATFIELD RC, EDWARDS PR, JOHNSON NM. Two unexpected deaths from pneumothorax. *Lancet* 1979; **1**: 356.
3. SHANAHAN MX, MONK I, RICHARDS HJ. Unilateral pulmonary oedema following re-expansion of pneumothorax. *Anaesthesia and Intensive Care* 1975; **3**: 19–30.
4. NOBLE WH. Pulmonary edema: a review. *Canadian Anaesthetists' Society Journal* 1980; **27**: 286–302.
5. SPRUNG CL, LOEWENHERZ JW, BAIER H, HAUSER MJ. Evidence for increased permeability in reexpansion pulmonary edema. *American Journal of Medicine* 1981; **71**: 497–500.
6. CRANDALL ED, STAUB NC, GOLDBERG HS, EFFROS RM. Recent developments in pulmonary edema: UCLA Conference. *Annals of Internal Medicine* 1983; **99**: 808–22.
7. FEIN A, GROSSMAN RF, JONES JG, OVERLAND E, PITTS I, MURRAY JF, STAUB NC. The value of edema fluid protein measurement in patients with pulmonary edema. *American Journal of Medicine* 1979; **67**: 32–8.
8. MAHAJAN VK, SIMON M, HUBER GL. Reexpansion pulmonary edema. *Chest* 1979; **75**: 192–4.
9. SAUTTER RD, DREHER WH, MACINDOE JH, MYERS WO, MAGNIN GE. Fatal pulmonary edema and pneumonitis after reexpansion of chronic pneumothorax. *Chest* 1971; **60**: 399–401.
10. TRAPNELL DH, THURSTON JGB. Unilateral pulmonary oedema after pleural aspiration. *Lancet* 1970; **1**: 1367–1369.
11. SHAW TJ, CATERINE JM. Recurrent re-expansion pulmonary edema. *Chest* 1984; **86**: 784–6.
12. MILLER WC, TOON R, PALAT H, LACROIX J. Experimental pulmonary edema following re-expansion of pneumothorax. *American Review of Respiratory Disease* 1973; **108**: 644–6.
13. ZISKIND MM, WELL H, GEORGE RA. Acute pulmonary edema following the treatment of spontaneous pneumothorax with excessive negative intrapleural pressure. *American Review of Respiratory Disease* 1965; **92**: 632–6.
14. PAVLIN DJ, CHENEY FW. Unilateral pulmonary edema in rabbits after reexpansion of collapsed lung. *Journal of Applied Physiology* 1979; **46**: 31.
15. BUCZKO GB, GROSSMAN RF, GOLDBERG M. Reexpansion pulmonary edema: evidence for increased capillary permeability. *Canadian Medical Association Journal* 1981; **125**: 460–1.
16. CORYLLOS PN, BIRNBAUM GL. Circulation in compressed, atelectatic and pneumonic lung (pneumothorax-apneumotosis-pneumonia). *Archives of Surgery* 1929; **19**: 1346–1424.
17. GOODALE RL, GOETZMAN B, VISSCHER MB. Hypoxia and iodoacetic acid and alveolocapillary barrier permeability to albumin. *American Journal of Physiology* 1970; **219**: 1226–30.
18. PAVLIN DJ, NESSLY ML, CHENEY FW. Increased pulmonary vascular permeability as a cause of reexpansion edema in rabbits. *American Review of Respiratory Disease* 1981; **124**: 422–7.
19. CHILDRESS ME, MOY G, MOTTRAM M. Unilateral pulmonary edema resulting from treatment of spontaneous pneumothorax. *American Review of Respiratory Disease* 1971; **104**: 119–21.
20. LEVINE BE, JOHNSON RP. Effects of atelectasis on pulmonary surfactant and quasi-static lung mechanics. *Journal of Applied Physiology* 1965; **20**: 859–64.
21. CARLSON RJ, CLASSEN KL, GOLLAN F, GOBBEL WG, SHERMAN DE, CHRISTENSEN RO. Pulmonary edema following the rapid reexpansion of a totally collapsed lung due to a pneumothorax: a clinical and experimental study. *Surgical Forum* 1958; **9**: 367–71.

Forum

Plasma catecholamine concentrations—changes after infiltration with local anaesthetic solutions and adrenaline during bat-ear surgery

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Summary

Plasma catecholamine concentrations were measured in 12 patients who had bilateral bat-ear surgery following infiltration of each ear with 2 ml 2% lignocaine with adrenaline 1:100 000. Venous blood samples were withdrawn before and at set intervals after infiltration. Plasma adrenaline concentration increased from 0.8 pmol/ml to a peak of 2.2 pmol/ml at 2 minutes after infiltration; this is an increase of 175%. There was no significant change in plasma noradrenaline concentration.

Key words

Anaesthetics, local; lignocaine.

Sympathetic nervous system; catecholamines, sympathomimetic agents.

Local anaesthetic solutions which contain adrenaline are used commonly for subcutaneous infiltration during surgery to reduce bleeding and improve surgical vision. Recommendations were made with regard to a 'safe' dose of adrenaline^{1,2} following several reports of ventricular dysrhythmias during such procedures.^{3,4} However, these recommendations did not consider the site of infiltration and more importantly were not substantiated by measurement of plasma adrenaline concentrations. To date there have been few studies which have examined the changes in plasma catecholamine concentrations following infiltration at various sites with adrenaline-containing solutions.

The present study was designed to measure the changes in plasma adrenaline concentration in response to exogenous administration during bilateral bat-ears' surgery under local anaesthesia and to examine concomitant changes in cardiac rhythm, heart rate and arterial pressure.

Method

The study was conducted on 12 ASA 1 patients (age 15–27 years and weight 45–80 kg) who had bilateral bat-ear surgery under local anaesthesia as day cases. Written informed consent was obtained for withdrawal of venous blood for measurement of plasma catecholamine concentrations.

The patients were unpremedicated and on arrival in the operating theatre an 18-gauge cannula (Venflon) was inserted in an antecubital fossa vein after local infiltration with 1% plain lignocaine. The ECG was displayed continuously and arterial pressure measured with an automatic pressure recorder (Copal). Baseline recordings of heart rate and arterial pressure were taken following a 5-minute rest period. Venous blood samples (10 ml) were obtained from the *in-situ* cannula at the same time. Each ear was then infiltrated with 2 ml 2% lignocaine with adrenaline

1:100 000. Heart rate and arterial pressure were measured and a venous blood sample obtained immediately after infiltration. This was repeated at 1, 2, 5, 10 and 15 minutes thereafter. Surgery did not start until the end of the study period.

Blood samples were centrifuged immediately and the plasma separated and stored at -70°C for future analysis. Plasma concentrations of adrenaline and noradrenaline were measured with high pressure liquid chromatography. The methodology and accuracy of the technique used in our laboratory have been described previously.⁵ The results were submitted to statistical analysis using paired Student's *t*-test following analysis of variance.

Results

Mean plasma adrenaline concentration increased from a baseline value of 0.8 pmol/ml to 2.1 pmol/ml ($p < 0.02$) immediately after infiltration of the ears. A peak of 2.2 pmol/ml ($p < 0.01$) was evident at 2 minutes post infiltration which represented an increase of 175% above the baseline value. Thereafter, the plasma adrenaline concentration declined but remained significantly higher than baseline value at 15 minutes (Fig. 1). There was no significant change in plasma noradrenaline concentration from the baseline value of 2.5 pmol/ml throughout the study.

No ventricular arrhythmias were detected on the ECG at any stage of the 15-minute period which followed local anaesthetic infiltration. However, there was a significant increase in heart rate ($p < 0.01$) from a baseline value of 78 beats/minute to a peak of 97 beats/minute immediately post infiltration (Fig. 2). In common with the trend in change of heart rate, systolic pressure increased from a baseline value of 120 mmHg to 130 mmHg after infiltration (time 0 minutes) ($p < 0.02$). There was no significant

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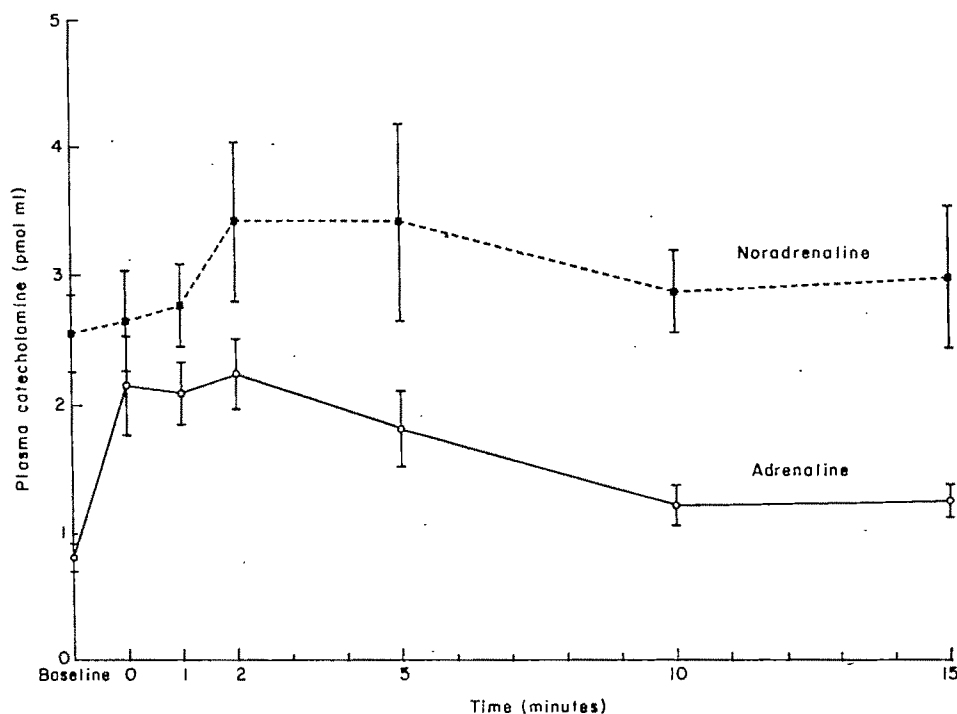


Fig. 1. Changes in plasma catecholamine concentration, mean (SEM), following submucous infiltration of the ears with 4 ml 2% lignocaine with adrenaline 1:100 000.

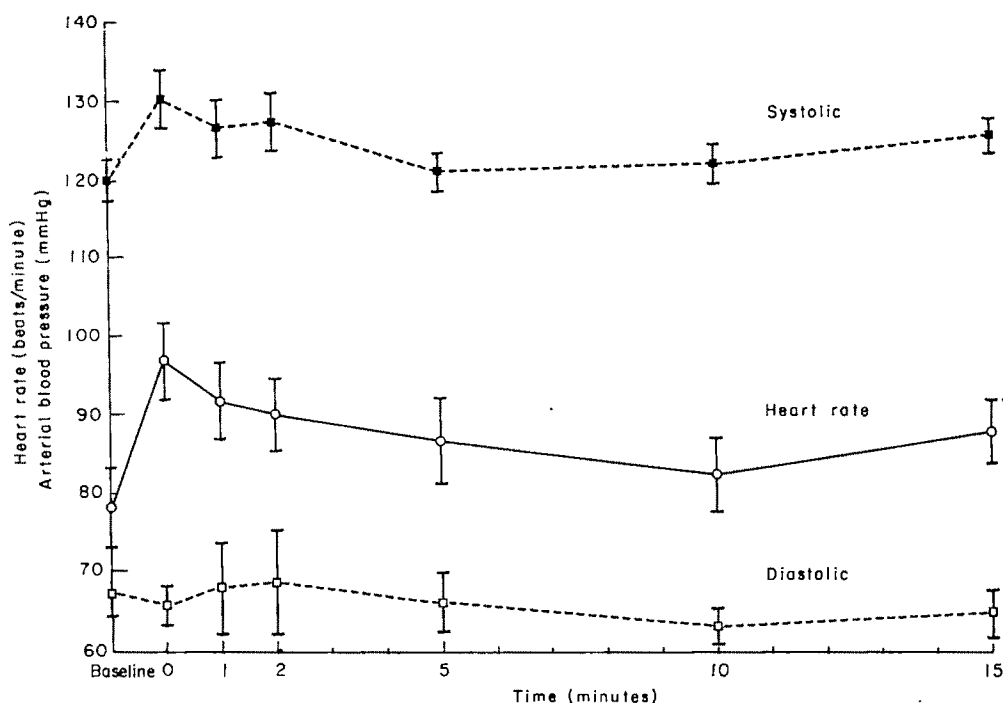


Fig. 2. Changes in heart rate, systolic and diastolic arterial pressure, mean (SEM), following submucous infiltration of the ears with 4 ml 2% lignocaine with adrenaline 1:100 000.

change in diastolic pressure throughout the period of study.

Discussion

This study has shown that there is very rapid systemic absorption of adrenaline following infiltration. A 163% increase in plasma adrenaline concentration was measured immediately after the use of 4 ml lignocaine 2% with

adrenaline 1:100 000 (40 μ g or 0.7 μ g/kg). The value was 175% greater than baseline at 2 minutes after infiltration. Some of this increase may have arisen from endogenous release of adrenaline as a result of sympathoadrenal activity of stress. However, this seems highly unlikely in the absence of a concomitant increase in noradrenaline, since stress responses to surgery and anaesthesia are accompanied normally by similar increases in plasma concentrations of both adrenaline and noradrenaline.⁶

The baseline concentrations of catecholamines in the present study were in the same range as those reported in previous studies,^{5,7,8} which adds further confidence to the significance of the increase in adrenaline following infiltration. Rapid systemic absorption of adrenaline has also been shown by other studies where adrenaline-containing solutions have been injected into highly vascular areas such as the nose and the mouth.

Donlon and Moss⁹ measured plasma catecholamine concentrations after eyelid infiltration and retrobulbar block with 2% lignocaine and adrenaline 1:200 000 for cataract extraction under local anaesthesia. The dose of adrenaline used was the same as that in the present study (0.7–0.8 µg/kg) and the plasma adrenaline concentration at 2 minutes was 2.2 pmol/ml which is also similar. Tolas *et al.*¹⁰ measured arterial plasma catecholamine concentrations during dental extraction under local anaesthesia. A dose of 18 µg adrenaline produced a two-fold increase in adrenaline at 3 and 5 minutes after infiltration. Taylor *et al.*¹¹ observed a 390% increase in plasma adrenaline concentration at 2 minutes after submucous infiltration with 20 µg adrenaline (0.4 µg/kg) in anaesthetised patients who had nasal surgery. In a separate study Cotton *et al.*⁸ observed a 566% increase in plasma adrenaline concentration at 2 minutes after nasal infiltration with 21 ml 0.5% lignocaine with adrenaline 1:200 000 (105 µg or 1.5 µg/kg). In contrast a separate group of patients who were given 200 µg adrenaline during an axillary brachial plexus block demonstrated a peak increase of only 112% which occurred 10 minutes after completion of the block. There was a statistically significant increase in heart rate and systolic arterial pressure although no serious dysrhythmias were detected.

Several authors have made recommendations regarding a 'safe' dose of adrenaline for infiltration in anaesthetised patients. Katz *et al.*³ proposed that the dose in adults should not exceed 10 ml of 1:100,000 (100 µg) in any given 10-minute period or 30 ml/hour during halothane anaesthesia and under conditions of normocapnia. Johnston *et al.*⁴ recommended a dose of 1 µg/kg as safe during halothane anaesthesia. Karl *et al.*¹² proposed that in children this could be increased to 10 µg/kg. It should be noted that these recommendations have not been substantiated by the measurement of plasma adrenaline concentration.

Unfortunately there are as yet no data available on the dysrhythmogenic threshold for plasma concentrations of catecholamines in man. Sumikawa *et al.*¹³ have shown that the threshold for ventricular dysrhythmias in dogs during halothane anaesthesia (1.2 MAC) was 230 pmol/ml. This was produced by an intravenous adrenaline infusion of 2.18 µg/kg/minute. However, this might not be applicable to man because of marked species difference. Cotton *et al.*⁸ have stressed that the so-called safe dose of adrenaline is meaningless unless the site of administration is specified. They believe that a plasma adrenaline concentration of 1.5–2.0 pmol/ml is possibly acceptable. In the present study the peak plasma adrenaline concentration was 2.24 pmol/ml

and if these authors' recommendations are correct we would conclude that the dose of adrenaline for bilateral bat-ear surgery should be restricted to 40 µg or 0.7 µg/kg (as used in the present study). However it should be noted that these statements may not be applicable to patients who receive volatile anaesthetic agents.

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References

1. KATZ RL, MATTEO RS, PAPPER EM. The injection of epinephrine during general anesthesia with halogenated hydrocarbons and cyclopropane in man. *Anesthesiology* 1962; **23**: 597–600.
2. JOHNSTON RR, EGER EI, WILSON C. A comparative interaction of epinephrine with enflurane, isoflurane and halothane in man. *Anesthesia and Analgesia* 1976; **55**: 709–12.
3. ROSEN M, ROE RB. Adrenaline infiltration during halothane anaesthesia. A report of two cases of cardiac arrest. *British Journal of Anaesthesia* 1963; **35**: 51–3.
4. VAREJES L. The use of solutions containing adrenaline during halothane anaesthesia. *Anaesthesia* 1963; **18**: 507–10.
5. DERBYSHIRE DR, CHMIELEWSKI A, FELL D, VATER M, ACHOLA KJ, SMITH G. Plasma catecholamine responses to tracheal intubation. *British Journal of Anaesthesia* 1983; **55**: 855–60.
6. DERBYSHIRE DR, SMITH G. Sympathoadrenal responses to anaesthesia and surgery. *British Journal of Anaesthesia* 1984; **56**: 725–39.
7. LOW JM, HARVEY JT, COOPER GM, PRENDIVILLE WJ. Plasma concentrations of catecholamines following adrenaline infiltration during gynaecological surgery. *British Journal of Anaesthesia* 1984; **56**: 849–53.
8. COTTON BR, HENDERSON HP, ACHOLA KJ, SMITH G. Changes in plasma catecholamine concentrations following infiltration with large volumes of local anaesthetic solution containing adrenaline. *British Journal of Anaesthesia* 1986; **58**: 593–97.
9. DONLON JV, MOSS J. Plasma catecholamine levels during local anaesthesia for cataract operation. *Anesthesiology* 1979; **51**: 471–3.
10. TOLAS AG, PFLUG AE, HALTER JB. Arterial plasma epinephrine concentrations and haemodynamic responses after dental injection of local anesthetic with epinephrine. *Journal of the American Dental Association* 1982; **104**: 41–3.
11. TAYLOR S, ACHOLA KJ, SMITH G. Plasma catecholamine concentrations. The effects of infiltration with local analgesics and vasoconstrictors during nasal operation. *Anaesthesia* 1984; **39**: 520–23.
12. KARL HW, SWEDLOW DB, LEE KW, DOWNES JJ. Epinephrine/halothane interactions in children. *Anesthesiology* 1983; **58**: 142–5.
13. SUMIKAWA K, ISHIZAKA N, SUZAKI M. Arrhythmogenic plasma levels of epinephrine during halothane, enflurane and pentobarbital anesthesia in the dog. *Anesthesiology* 1983; **58**: 322–5.

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Propofol: clinical strategies for preventing the pain of injection

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Summary

Eight modes of administration of propofol were assessed in order to minimise the pain of injection. An intravenous bolus injection in the antecubital fossa was the only approach that caused no pain. When administered intravenously in the dorsum of the hand the pain score and the number of patients who experienced pain was reduced significantly by mixing the agent with lignocaine when compared with a bolus injection. Slowing the speed of injection caused the greatest discomfort. An indirect biochemical mechanism for the pain is proposed.

Key words

Anaesthetics, intravenous; propofol.

Complications; pain.

The initial investigations with 2:6 di-isopropyl phenol (propofol) were carried out with a formulation which contained Cremophor. The drug was found to be a satisfactory induction agent in a dose of 2.0 mg/kg but frequently caused pain on injection when given intravenously in the dorsum of the hand.¹ In view of the association between agents which contained Cremophor and anaphylactoid reactions^{2,3} an emulsion formulation of the drug was developed. This formulation has not eliminated the injection pain although the results are said to be slightly better than with the Cremophor preparation.⁴ Nevertheless, when propofol in an oil emulsion is administered through an intravenous catheter in the dorsum of the hand the incidence of pain may still be as high as 45%.⁵

Premedication appears to have little effect on the incidence⁴ but may reduce the severity of pain.⁶ The site of injection, however, does seem to be important. Several studies have reported less pain when propofol is injected into a vein in the antecubital fossa.^{4,7,8,9} Other authors have described administration of lignocaine either prior to^{8,9} or mixed freshly with propofol to reduce this discomfort.¹⁰ This study was designed to assess different modes of administration in order to minimise the injection pain.

Method

The patients gave ethically approved informed consent. One hundred and twenty (ASA classes 1 or 2) patients were assigned randomly to one of eight groups (see Table 1). The patients were aged 16–70 years, weighed 40–95 kg, and were to undergo daycase surgery. No premedication was administered. In all groups except V and VII general anaesthesia was induced with propofol 2.5 mg/kg intravenously through a 23-gauge Butterfly (Abbot) needle in the dorsum of the hand. Group I received only propofol as a bolus at a rate of approximately 2 ml/second. Group II

patients received 1% lignocaine 1 ml intravenously followed by a propofol bolus through the same vein 30 seconds later. Group III received the same dose of lignocaine but followed by a propofol bolus 120 seconds later. In Group IV, 1% lignocaine 1 ml was mixed with propofol 200 mg. The patients then received a propofol/lignocaine bolus 2.5 mg/kg. Patients in Group V received a propofol bolus through a 23-gauge Butterfly needle in the antecubital fossa. Group VI patients had a venous tourniquet applied at the wrist and 1% lignocaine 1 ml injected intravenously. This was followed 120 seconds later by a propofol bolus and a simultaneous release of the tourniquet. A 16-gauge intravenous catheter was placed in the dorsum of the hand in patients in Group VII. Propofol was subsequently administered through a fast-flowing intravenous infusion of dextrose 5% BP. Group VIII received propofol 2.5 mg/kg administered slowly over 75 seconds.

At the start of injection patients were asked to report any discomfort and classify pain as being absent, mild, moderate or severe. The degree of pain was subsequently scored as: no pain, 0; mild pain, 1; moderate pain, 2; severe pain, 3.

Results

There was no significant distribution difference in age, sex or weight between the eight groups. The mean pain score for each group and the numbers who experienced pain are summarised in Table 1.

An intravenous bolus injection in the antecubital fossa was the only approach that caused no pain. The pain score and the number who experienced pain was, however reduced significantly ($p < 0.05$; Mann-Whitney *U*-Test) by a mixture of propofol and lignocaine (Group IV) when compared with a propofol bolus (Group I). Slowing the speed of injection (Group VIII) caused the greatest discomfort.

Table 1. Pain score and number with pain in each group

Group	Number in group	Mode of administration	Mean (SD) pain score	Number with pain
I	15	Propofol bolus only	0.93 (1.09)	7
II	15	1% lignocaine 1 ml intravenously, propofol bolus 30 seconds later	0.66 (0.89)	6
III	15	1% lignocaine 1 ml intravenously, propofol bolus 120 seconds later	1.4 (1.05)	11
IV	15	1% lignocaine 1 ml mixed with propofol 200 mg intravenously, propofol bolus 2.5 mg/kg	0.13 (0.35)	2*
V	15	Propofol bolus through 23-G Butterfly needle antecubital fossa	0	0
VI	15	Venous tourniquet at wrist, 1% lignocaine 1 ml intravenously, propofol bolus and release of tourniquet 120 seconds later	0.6 (0.73)	7
VII	15	16-G intravenous catheter, dorsum of hand, propofol bolus in fast flowing intravenous infusion	1.26 (1.03)	11
VIII	15	Propofol only, 75 second injection	1.66 (0.81)	13

* $p < 0.05$ when compared with group I.

Discussion

The solvent used to solubilize nonwater soluble drugs can play an important role in both acute and long-term venous tolerance¹¹ and prevent the active agent from dissolving and irritating the endothelial layer of the vein.¹² The use of a fat emulsion with diazepam was a major advance for it abolished the pain of injection^{13,14} and reduced the incidence of thrombophlebitis.

The results of this study and others suggest that the use of a fat emulsion with propofol has little effect on the incidence of injection pain. Post injection thrombophlebitis, however, does not appear to be a problem.¹⁵

No pain was reported when the drug was injected into a large vein in the antecubital fossa. This is presumably because the drug comes into the mid-stream in the lumen of the vein and its contact with the sensitive vein wall in high concentration will be minimal. The drug may also be buffered effectively by blood with which it can mix freely.¹⁵ On this basis, however, it is difficult to explain why a slow (75 second) injection of propofol should cause more pain than a rapid bolus. Perhaps the duration of exposure to the vein wall is of more importance as a cause of discomfort than with a rapid bolus where the high concentration of drug is quickly cleared from the vein and replaced with blood. Also in very small veins there is probably little difference in propofol concentration between a rapid bolus and a 75 second injection as the vein may expand to accommodate the different flow rates. The vein wall may be exposed to a similar propofol concentration but for a longer period of time with the slower injection rate. This hypothesis is compatible with the observation that the pain which follows injection is not usually immediate in onset and suggests it may not be a direct effect at all but involves some mediator such as a kininogen.

In animal studies with propofol there seems to be a species variability in the sensitivity to an intravenous injection. The rat model was noted to struggle during injection and an associated pressor response, which could be attenuated with fentanyl, was observed. However, injection into the rabbit ear vein, which is usually a sensitive test for detecting venous irritation, provoked minimal response. Similarly little response was noted during intravenous injection into cats, dogs or pigs. This species variability suggests there is a process involved which is not attributable to every animal, such as a kinin cascade. A direct irritant effect would not have this between-species variation. It may also account for the between-patient variability since some patients do not have the same level to trigger this system.

It is not at all clear why lignocaine mixed freshly with propofol causes less pain than when administered prior to propofol, but the findings of this study concur with those of Brooker et al.¹⁰ They reported that lignocaine in a propofol emulsion reduced the pain to approximately 7% whereas the incidence of pain was not reduced by prior lignocaine administration. It may be that lignocaine acts as a stabiliser for a kinin cascade. Lignocaine injected prior to propofol may be washed away in the blood before the propofol bolus, which makes less lignocaine available to act in close association with this mediator.

Brooker's study was complicated slightly by its use of a variable premedication, a variable pre-induction opioid and opioid dose, and by not establishing a control without premedication, or pre-induction opioid, and without lignocaine. These investigators observed, however, that in some cases where the propofol/lignocaine mixture had not been made up freshly the patients did complain of pain. They

concluded in collaboration with the manufacturers that the emulsion should not be regarded as stable for more than 30 minutes after mixing since lignocaine may move into the lipid phase after mixing and diminishes progressively the free effective concentration.

In conclusion it appears that the most effective way to reduce the pain of injection is to inject through a large vein in the antecubital fossa. Alternatively propofol mixed freshly with lignocaine prior to injection will also reduce the pain incidence. The chemical basis for the pain has still to be elucidated.

Acknowledgments

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References

- BRIGGS LP, CLARKE RSJ, DUNDEE JW, MOORE J, BAHER M, WRIGHT PJ. Use of di-isopropyl phenol as main agent for short procedures. *British Journal of Anaesthesia* 1981; **53**: 1197-1202.
- CLARKE RSJ, DUNDEE JW, GARRET RT, MCARDLE GK, SUTTON JA. Adverse reactions to intravenous anaesthetics. A survey of 100 reports. *British Journal of Anaesthesia* 1975; **47**: 575-85.
- BRIGGS LP, CLARKE RSJ, WATKINS J. An adverse reaction to the administration of disopropofol ('Diprivan'). *Anaesthesia* 1982; **37**: 1099-101.
- BRIGGS LP, WHITE M. The effects of premedication on anaesthesia with propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 35-7.
- UPPINGTON J, KAY NH, SEAR JW. Propofol ('Diprivan') as a supplement to nitrous oxide oxygen for the maintenance of anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 80-3.
- BILAINE J, DESMONTS JM. Effects of premedication with atropine or hydroxyzine on induction and maintenance of anaesthesia with propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 38-9.
- KNELL PJW, MCKEAN JF. An investigation of the pharmacokinetic profile of propofol ('Diprivan') after administration for induction and maintenance of anaesthesia by repeat bolus doses in patients having spinal anaesthetic block. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 60-1.
- LEES NW, MCCULLOCH M, MAIR WB. Propofol ('Diprivan') for induction and maintenance of anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 88-9.
- STARK RD, BINKS SM, DUTKA VN, O'CONNOR KM, ARNSTEIN MJA, GLEN JB. A review of the safety and tolerance of propofol ('Diprivan'). *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 152-6.
- BROOKER J, HULL CJ, STAFFORD M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia* 1985; **40**: 91-2.
- OLESEN AS, HÜTTEL MS. Local reactions to I.V. diazepam in three different formulations. *British Journal of Anaesthesia* 1980; **52**: 609-11.
- JUSKO WJ, GRETCH M, GASSET R. Precipitation of diazepam from intravenous preparations. *Journal of the American Medical Association* 1973; **225**: 176.
- VON DARDEL O, MEBIUS C, MOSSBERG T. Diazepam in emulsion form for intravenous usage. *Acta Anaesthesiologica Scandinavica* 1976; **20**: 221-4.
- MATTILA MAK, SUISTOMAA M. Intravenous premedication with diazepam. *Anaesthesia* 1984; **39**: 879-882.
- MATTILA MAK, KOSKI EMJ. Venous sequelae after intravenous propofol ('Diprivan')—a comparison with methohexitone in short anaesthesia. *Postgraduate Medical Journal* 1985; **61** (Suppl. 3): 162-4.

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Nifedipine prevents the pressor response to laryngoscopy and tracheal intubation in patients with coronary artery disease

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Summary

The efficacy of sublingual nifedipine, administered one minute before anaesthetic induction, in order to minimise the pressor response to laryngoscopy and tracheal intubation was studied in a group of 15 patients who underwent coronary artery bypass surgery. Another group of 15 similar patients served as control. Premedication consisted of oral diazepam 5–10 mg, intramuscular morphine 0.2 mg/kg and promethazine 0.4 mg/kg. Anaesthesia was induced with morphine 0.1–0.15 mg/kg and thiopentone 3–5 mg/kg. Laryngoscopy and tracheal intubation were facilitated with suxamethonium 1.5 mg/kg. A significant increase in blood pressure occurred during and after laryngoscopy and tracheal intubation in the control group. This increase was absent in the patients pretreated with nifedipine. The nifedipine group also maintained a lower rate-pressure-product than the control group during the period of study. It is concluded that nifedipine 10 mg is a useful pretreatment to prevent the pressor response to laryngoscopy and tracheal intubation in patients with coronary artery disease.

Key words

Complication; sympathetic stimulation.

Pharmacology; calcium antagonists; nifedipine.

Reflex tachycardia and hypertension during laryngoscopy and tracheal intubation occur frequently in lightly anaesthetised patients.^{1–3} These changes are usually transient and have no deleterious consequences, but in some patients they can cause serious problems such as myocardial ischaemia and (or) left ventricular failure as a result of increased myocardial oxygen requirements.⁴ Patients with pre-existing hypertension and/or coronary artery disease are particularly at risk.^{4,5}

Nifedipine, a potent coronary and peripheral vasodilator, is used increasingly for the treatment of angina and hypertension.⁶ We have found sublingual nifedipine 10 mg to be effective in preventing this response, in a preliminary trial in patients without cardiovascular disease (unpublished data). The present study was conducted to evaluate sublingual nifedipine as a safeguard against the haemodynamic responses to laryngoscopy and tracheal intubation in patients who undergo coronary artery bypass surgery, since the absence of a pressor response has more significance in patients with pre-existing hypertension or coronary artery disease.

Method

Thirty patients aged 40–60 years of either sex who required coronary artery bypass surgery were admitted to the study. Informed consent was obtained from all of them. They were allocated, on arrival in the operating theatre, to one of two groups of 15 each with the help of a random chart. The patients did not receive their normal medication on the day of surgery.

Premedication consisted of diazepam 5–10 mg orally 2 hours before anaesthesia, morphine 0.2 mg/kg and promethazine 0.4 mg/kg intramuscularly one hour before anaesthesia. One of the two groups (group 2) received sublingual nifedipine 10 mg, one minute before induction.

Anaesthesia was induced with morphine 0.1–0.15 mg/kg given intravenously followed by thiopentone 3–5 mg/kg in order to obtund the eyelash reflex. This was followed by suxamethonium 1.5 mg/kg. All induction drugs were administered within 4–6 minutes. Laryngoscopy and tracheal intubation were performed, after the onset of apnoea, and took not more than 30 seconds. Ventilation of the lungs was assisted/controlled with 40% oxygen in nitrous oxide delivered through a semiclosed system with soda-lime, with a fresh gas flow rate of 70 ml/kg during the period of study.

All patients were monitored from the time of their arrival in the operating theatre with direct blood pressure measurement, from a cannula inserted in a radial artery. The ECG was displayed on an oscilloscope using left-sided chest leads. Samples for arterial blood gas analysis were withdrawn before induction and once during the investigation to ensure adequate ventilation. Records of systolic arterial pressure, diastolic arterial pressure and heart rate were obtained in the pre-induction period, before any drug was administered (control readings), during laryngoscopy (time zero) and then at one, 3 and 5-minute intervals thereafter (Table 2). Heart rate and blood pressure were recorded by a worker who was not aware of the study treatment group. All the patients were intubated in the between time zero and time one. Surgical stimulus or analgesic supplements were avoided during the period of recording blood pressure and heart rate. Undue increases in blood pressure after tracheal intubation, if any, were controlled with halothane supplements. Inhalational agents were otherwise avoided during the period of study.

Mean arterial pressure was calculated by the formula; $MAP = 1/3 (SAP + 2 DAP)$ and the rate-pressure-product (RPP) was calculated by the formula $RPP = SAP \times HR$. Student's *t*-test for paired observations was used for analysis within the group and that for unpaired observations for analysis between the groups.

Results

The pre-induction patient data were comparable in both the groups (Table 1).

Heart rate. There was a significant rise in heart rate (HR) in both the groups at 0, 1 and 3 minutes after commencement of laryngoscopy (Table 2). By 5 minutes the HR in both the groups had reached levels not significantly higher than the basal levels. The HR values of the control group did not differ significantly from the nifedipine group at any time during the investigation ($p > 0.05$).

Arterial blood pressure. A significant increase in systolic arterial pressure (SAP) was seen at 0, 1 and 3-minute intervals and a significant increase in mean arterial pressure (MAP) was seen at 0 and 1-minute intervals—in the control group (Table 2). Blood pressure did not increase above the basal levels at any time during the investigation, in the nifedipine group. Between-group analysis reveals significantly higher readings of SAP and MAP at 0 and 1-minute intervals in the control group when compared with the nifedipine group (Table 2). Ten of the 15 patients in the control group required halothane for the control of post-intubation increase in arterial blood pressure. This was not required in any of the patients in nifedipine group.

Rate-pressure-product. A significant rise in RPP occurred in both groups at 0 and 1-minute intervals. At the 3-minute interval RPP had reached basal levels in the nifedipine group while it was still high in the control group (Table 2). Between-group analysis revealed the RPP in the nifedipine group was significantly lower than that in control group throughout the investigation.

ECG. No evidence of dysrhythmia or ischaemia was seen in any of the patients in either groups.

Discussion

Our results indicate that sublingual nifedipine administered 5–7 minutes before laryngoscopy and tracheal intubation prevents the reflex rise in arterial blood pressure. Also it minimises the rise in RPP during this period.

The increase in arterial pressure during laryngoscopy and tracheal intubation is associated with a rise in nor-adrenaline concentration,^{7,8} which suggests increased sympathetic nervous activity. This pressor response may lead to a number of complications which include myocardial ischaemia,^{3,9} cardiac failure and intracranial haemorrhage,⁴ and increases in intracranial pressure.¹⁰ Methods to inhibit the reaction to the painful stimulus of laryngoscopy and intubation should be effective in suppressing the pressor response. A number of drugs have been recommended. These include on the afferent side; topical lignocaine,³ volatile agents,¹¹ narcotic analgesics,^{12–14} midazolam¹⁵ and intravenous lignocaine,¹⁶ and on the efferent side; ganglion blockers,¹⁷ beta-adrenergic blockers,¹⁸ and vasodilators.^{19–21} However, only a few of these pharmacological approaches have been found to be satisfactory because they are only partially effective or the agents used may be too long-acting or have other undesirable side effects.

Nifedipine is a calcium antagonist and in the dose used in this study causes moderate dilatation of coronary and peripheral vessels without affecting myocardial contractility or conduction.²² Thus when administered sublingually it improves coronary blood flow and reduces arterial blood pressure with a slight increase in cardiac output.^{16,22} None of the previous pharmacological agents (see above), except nitroglycerine, used for preventing the pressor response to laryngoscopy and tracheal intubation, offers these advantages which are of special importance in patients with pre-existing coronary artery disease. Recently nitroglycerine has

Table 1. Pre-induction patient data (mean, SEM) in both the groups.

	Group 1 <i>n</i> = 15	Group 2 <i>n</i> = 15
Age range	41–60	40–60
Age, years	52 (3.6)	53.5 (4)
Males:females	13:2	13:2
Weight range	50–81	53–85
Weight, kg	65.9 (3.9)	67 (3.5)
HR (beats/minute)	82.9 (2.6)	85.6 (3.3)
SAP (mmHg)	128 (3.7)	126.8 (3.9)
DAP (mmHg)	80 (2.3)	78.35 (2.8)
Ejection fraction, percent	55 (2.8)	55.5 (3.2)
Patients with beta blockers	7	9
Patients with calcium antagonists	9	10
Patients with treated hypertension	6	8

Table 2. Change in HR, SAP, MAP and RPP at various intervals in different groups. Values expressed as mean (SEM).

		Pre-induction	After laryngoscopy (minutes)			
			0	1	3	5
Heart rate	Group 1 (control)	82.9 (10.1)	104† (9.8)	104.6‡ (11.1)	95.8* (12.8)	87.5 (10.6)
	Group 2 (nifedipine)	85.6 (12.7)	101‡ (13.6)	102.8‡ (14.7)	96* (12.9)	92.5 (8.9)
Systolic arterial pressure	Group 1	128 (14.4)	145.3‡ (15.4)	146.7‡ (20.0)	136* (18.3)	133.8 (13.3)
	Group 2	126.8 (15.3)	129.6¶ (25.4)	125.4¶ (25.2)	123¶ (20.8)	122.3§ (16.2)
Mean arterial pressure	Group 1	96 (9.2)	109.4‡ (12.8)	110.8‡ (14.7)	97.9 (8.6)	98 (9.6)
	Group 2	94.5 (7.6)	96.2¶ (11.2)	93.1§§ (9.8)	94 (8)	94.2 (9.2)
Rate pressure product	Group 1	10 650.2 (2275)	15 229‡ (1814)	15 438.7‡ (1507)	13 128† (1362)	11 607.5 (1738)
	Group 2	10 945.6 (2840)	13 089.6†§§ (3088)	12 750.8†§§ (4484)	11 900.6§ (2203)	12 285.3 (2527)

* $p < 0.05$ compared with pre-induction value within same group.
† $p < 0.01$ compared with pre-induction value within same group.
‡ $p < 0.001$ compared with pre-induction value within same group.
§ $p < 0.05$ compared with control group.
§§ $p < 0.01$ compared with control group.
¶ $p < 0.001$ compared with control group.

been shown to be an effective attenuator of the pressor response to laryngoscopy and intubation in patients who have coronary artery bypass surgery.²³ From our data it appears that nifedipine can also be used for the same purpose. None of our patients in the treatment group had undue hypotension during induction. However, nifedipine like any other vasodilator can produce hypotension especially in the hypovolaemic patient. It also has an additive dilating effect on peripheral vessels when used along with halothane.⁶ Thus, inhalational agents should be used with caution and in lesser concentrations in patients who have been pretreated with nifedipine.

Finally, we conclude that sublingual nifedipine administered 5–7 minutes before tracheal intubation is a safe, convenient and effective way to prevent the pressor response associated with laryngoscopy and intubation in patients with pre-existing coronary artery disease.

References

- KING BD, HARRIS LC JR, GREIFENSTEIN FE, ELDER JD JR, DRIPPS RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. *Anesthesiology* 1951; **12**: 556–66.
- FORBES AM, DALLY FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *British Journal of Anaesthesia* 1970; **42**: 618–24.
- STOELTING RK. Circulatory changes during direct laryngoscopy and tracheal intubation. Influence of duration of laryngoscopy with or without prior lidocaine. *Anesthesiology* 1977; **47**: 381–4.
- FOX EJ, SKLAR GS, HILL CH, VILLANUEVA R, KING BD. Complications related to pressor response to endotracheal intubation. *Anesthesiology* 1977; **47**: 524–5.
- PRYS-ROBERTS C, GREENE LT, MELOCHE R, FOËX P. Studies of anaesthesia in relation to hypertension. II: Haemodynamic consequences of induction and endotracheal intubation. *British Journal of Anaesthesia* 1971; **43**: 531–47.
- JONES RM. Calcium antagonists. In: ATKINSON RS, ADAMS AP, eds. *Recent advances in anaesthesia and analgesia*: 15. London: Churchill Livingstone, 1986: 89–106.
- RUSSELL WJ, MORRIS RG, FREWIN DB, DREW SE. Changes in plasma catecholamine concentrations during endotracheal intubation. *British Journal of Anaesthesia* 1981; **53**: 837–9.
- LOW JM, HARVEY JT, PRYS-ROBERTS C, DAGNINO J. Studies of anaesthesia in relation to hypertension. VII: Adrenergic responses to laryngoscopy. *British Journal of Anaesthesia* 1986; **58**: 471–7.
- ROY WL, EDELIST G, GILBERT B. Myocardial ischemia during non-cardiac surgical procedures in patients with coronary artery disease. *Anesthesiology* 1979; **51**: 393–7.
- BURNEY RB, WINN R. Increased cerebrospinal fluid pressure during laryngoscopy and intubation for induction of anaesthesia. *Anesthesia and Analgesia Current Researches* 1975; **54**: 687–90.
- SØRENSEN MB, JACOBSEN E. Pulmonary hemodynamics during induction of anaesthesia. *Anesthesiology* 1977; **46**: 246–51.
- DAHLGREN N, MESSETER K. Treatment of stress response to laryngoscopy and intubation with fentanyl. *Anaesthesia* 1981; **36**: 1022–6.
- KAUTTO UM. Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. *Acta Anaesthesiologica Scandinavica* 1982; **26**: 217–21.
- MARTIN DE, ROSENBERG H, AUKBURG SJ, BARTKOWSKI RR, EDWARDS MW, GREENHOW DE, KLINELING PL. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesthesia and Analgesia* 1982; **61**: 680–4.
- BORALESSA H, SENIOR DF, WHITWAM JG. Cardiovascular response to intubation. A comparative study of thiopentone and midazolam. *Anaesthesia* 1983; **38**: 623–7.
- ABOU-MADI M, KESZLER H, YACOB O. A method for prevention of cardiovascular reactions to laryngoscopy and intubation. *Canadian Anaesthetists' Society Journal* 1975; **22**: 316–29.
- DE VAULT M, GRIEFENSTEIN FE, HARRIS LC. Circulatory responses to endotracheal intubation in light general anaesthesia—the effect of atropine and phentolamine. *Anesthesiology* 1960; **21**: 360–2.
- PRYS-ROBERTS C, MELOCHE R, FOËX P. Studies of anaesthesia in relation to hypertension. I: Cardiovascular responses of treated and untreated patients. *British Journal of Anaesthesia* 1971; **43**: 122–37.
- STOELTING RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitropruside. *Anesthesia and Analgesia* 1979; **58**: 116–9.
- DAVIES MJ, CRONIN KD, COWIE RW. The prevention of hypertension at intubation. A controlled study of intravenous hydralazine on patients undergoing intracranial surgery. *Anaesthesia* 1981; **36**: 147–52.
- FASSOULAKI A, KANIARIS P. Intranasal administration of nitroglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea. *British Journal of Anaesthesia* 1983; **55**: 49–52.
- KATES RA, KAPLAN JA. Calcium channel blocking drugs. In: KAPLAN JA, ed. *Cardiac Anesthesia. Vol 2 Cardiovascular pharmacology*. New York: Grune and Stratton Inc. 1984: 209–42.
- DICH-NIELSEN J, HOLE P, LANG-JENSEN T, OWEN-FALKENBERG A, SKOVSTED P. The effect of intranasally administered nitroglycerine on the blood pressure response to laryngoscopy and intubation in patients undergoing coronary artery by-pass surgery. *Acta Anaesthesiologica Scandinavica* 1986; **30**: 23–7.

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High frequency jet ventilation in intensive care—a review of 63 patients

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Summary

High frequency jet ventilation has been used clinically in this unit for over 2 years. During this time we have treated 63 intensive care patients for whom the mean duration of ventilatory support was 3.4 days, which represents more than 5000 patient hours in total, with the Penlon Bromsgrove humidified jet ventilator. The series comprises a wide variety of general intensive care patients; a review of these cases is presented.

Key words

Ventilation; high frequency jet.
Intensive care.

Mechanical ventilation of the lungs has been used increasingly over the last two decades to maintain gaseous exchange in cases of respiratory failure and is now the largest single indication for admission to our intensive care unit. Conventional intermittent positive pressure ventilation (IPPV), despite its increased sophistication, is still associated with considerable disturbance of the cardiovascular, respiratory, renal and nervous systems. These adverse effects are more important in the critically ill patient than in the otherwise healthy patient.

High frequency jet ventilation (HFJV) has been used clinically and experimentally for almost a decade;¹ its physiology has been reviewed by several authors.²⁻³ The advantages claimed for it include improved cardiovascular stability⁴ lower peak and mean airway pressures,⁵ preservation of renal function,² reduced sedation requirements⁶ and improved patient tolerance.⁷ To achieve adequate gaseous exchange with minimal cardiovascular and pulmonary compromise is clearly attractive to the ICU clinician. We therefore began an open-ended study of HFJV in critically ill patients in 1983.

Patient selection and methods

The study was approved by the hospital ethical committee and by the duty consultant anaesthetist for each individual patient. The diversity of pathology which presents in an intensive care unit makes rigid entry criteria to a study of this nature impracticable, so we adopted a flexible, broad-based approach:

Arterial hypoxaemia unresponsive to conventional IPPV techniques. ($\text{PaO}_2 < 10 \text{ kPa}$ despite 100% oxygen and the use of PEEP.)
High barotrauma risk.
Significant ventilator-related cardiovascular depression.
Significant pulmonary air leak.
Upper airway obstruction.

All five entry criteria were dependent on the clinical judgment of the anaesthetist in charge of the patient; upper airway management problem was added with the development of percutaneous techniques for HFJV.⁸ The study was not confined to any age group and exit criteria consisted of successful weaning from HFJV or death whilst on HFJV.

The ventilator. No suitable high frequency jet ventilator was commercially available in the UK which satisfied our requirements in terms of volume output, fail safe and alarm systems, simplicity of operation and humidification at the time of inception of this study. We therefore developed, in collaboration with Penlon Ltd., a purpose-built machine which is now available as the Penlon Bromsgrove Humidified jet ventilator.⁹ A prototype was used throughout this study and a brief summary of its operating capabilities is given in Table 1.

Ventilator settings. HFJV was initiated at a rate of 120 breaths/minute (bpm) (2Hz) in all cases. Driving pressure was adjusted to produce a tidal volume of 2.5 ml/kg body weight, with an inspiratory time fraction of 35% of total cycle time, i.e. 0.175 seconds.⁹ These variables were ad-

Table 1. Specification of Bromsgrove high frequency jet ventilator.

Parameter	Minimum	Maximum	Units
Minute volume	2	50	litres/minute
Tidal volume	10	1000	ml
Inspiratory time	10	60	% of cycle time
Respiratory frequency	50	200	breaths/minute
Driving pressure	20	400	kPa
Airway pressure alarm limits	0	6.0	kPa
Water flow	0.3	3.0	ml/minute
Inspired O ₂ concentration	21	100	%

Table 2. Presentation, duration of HFJV and outcome of series.

Diagnosis	Number of patients	Survivors	(% survival)	Mean duration of HFJV (days)
Postoperative respiratory failure	13	11	84	3.8
Septicaemia	9	5	55	3.7
Cor pulmonale	7	7	100	4.3
Major air leak	7	4*	57*	5.2
Primary pneumonia	6	5	83	4.6
Post cardiac arrest (proven myocardial infarct)	5	3	60	3.1
Cardiogenic shock†	4	2	50	1.8
Pulmonary embolus	3	1	33	0.9
Post cardiopulmonary bypass hypoxaemia	3	2	66	2.2
Upper airway obstruction‡	2	2	100	0.2
Status asthmaticus	2	2	100	0.6
Blown bronchial stump	1	1	100	0.4
Tracheo-oesophageal fistula	1	1	100	2.3
Totals	63	46	73	3.4

* Air leak stopped in all cases. Three patients died of non-respiratory pathology.
† Cardiac output less than 1.8 litres/sq m/minute.
‡ Direct tracheal puncture technique—see text.

justed according to the results of serial blood gas analyses. The humidifier water flow control was set to deliver between 30 and 45 mg of water per litre of driving gas.⁹

Delivery systems. Three delivery systems were employed, according to clinical requirements: the Mallinkrodt Hi-Lo jet tube (National Catheter Corporation), the jet mini-tracheostomy tube (Portex Ltd.), and a simple plastic intravenous cannula (12–18 gauge) for direct tracheal puncture techniques (Figs 1 and 2). The high minute

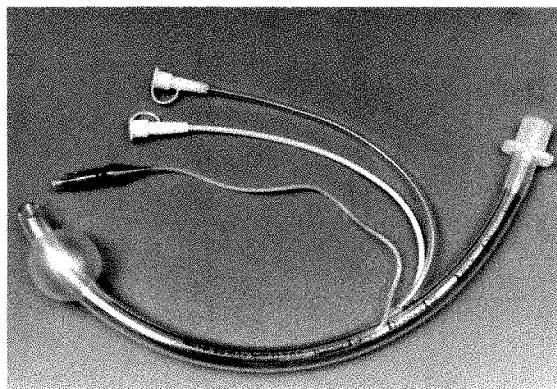


Fig. 1. Jet ventilation tracheal tube shown from above: airway pressure monitoring line (opaque tube); jet ventilation line and pilot line for the tube cuff.

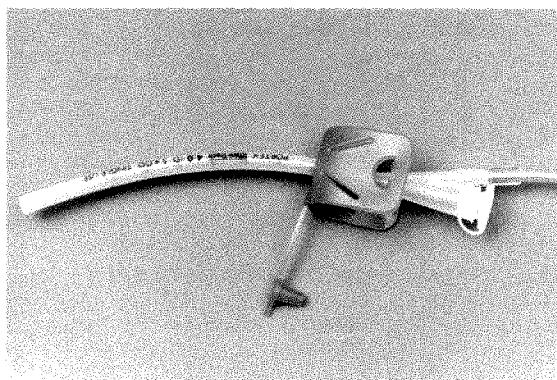


Fig. 2. The prototype jet ventilation minitracheostomy tube which shows the jet delivery line entering from the right, and immediately below it the suction port with its stopper in place.

volume capabilities of the ventilator avoid the need to use entrainment systems to augment tidal and minute volumes. Entrainment fraction is extremely difficult to predict in clinical practice because it depends primarily upon the design of the delivery system, the driving pressure used and compliance.⁹ Whenever possible we actively prevented entrainment by the use of a one-way expiratory valve attached to the catheter mount fixed to the tracheal tube. Prevention of entrainment is not possible, however, with the jet ventilation minitracheostomy or with the direct tracheal puncture techniques. The prehumidification of gas pulses also dispenses with the need for entrainment systems for humidification⁹ which allows the patient delivery line of the ventilator to be attached directly to the delivery system.

Data collection. All patients were stabilised on conventional IPPV for a minimum of 4 hours and were observed and monitored according to unit policy and their clinical condition. In addition arterial, central venous and, when available, pulmonary artery samples were taken for blood gas analysis and shunt calculation. In seven patients airway, oesophageal and intrathoracic pressures (from chest

drain tubes) were measured, and repeated after initiation of HFJV at clinically appropriate intervals. In 36 cases crossover studies with conventional IPPV were undertaken (IPPV–HFJV–IPPV), and on return to IPPV all variables were compared with the initial findings during IPPV. Four patients who showed significant clinical changes from their initial values were excluded, which left 32 in the crossover study.

Mixed airway oxygen tensions were measured while on HFJV by polarographic analysis of gas samples drawn from the main bronchi, in order to compensate for any air entrainment that occurred for the minitracheostomy and direct tracheal puncture techniques. At the high minute volumes used during HFJV (typically 15–25 litres/minute) the difference between the mixed airway oxygen tension and the true inspired oxygen tension is insignificant, approximately 2% at the relatively high delivered oxygen concentrations required in the patients in this series. Analysis was performed directly on the driving gas for the jet tracheal tube, a small sample of which is delivered to a port at the rear of the ventilator.⁹

Results

The presenting diagnosis, outcome and mean period of ventilation for the series as a whole is given in Table 2.

Oxygenation. HFJV produced acceptable oxygenation ($P_{aO_2} > 10$ kPa) in all but seven patients. Of these, four suffered from severe cardiogenic shock, two from major pulmonary embolus and one from severe bilateral chest consolidation, all of whom died of their underlying pathology. Calculated shunt volume was used to assess relative improvement in arterial blood gas oxygen tensions to allow for variation in F_{iO_2} , with the Comroe simplification¹⁰ and standard shunt equation¹¹ where pulmonary arterial samples were available, or virtual shunt¹¹ when such samples could not be obtained.

For the series as a whole mean shunt levels were 36% (range 15–56%) for IPPV and 23% (8–36%) for HFJV. The reduction in shunt is statistically significant ($p < 0.01$). The improvement in oxygenation after HFJV was marked in nine cases in whom mean shunt values fell by more than 20% (Table 3). These patients had impaired right ventricular function with central venous pressure (CVP) greater than 15 mmHg; right ventricular strain pattern on the ECG, in association with a low cardiac output, measured either by flow-directed pulmonary artery catheters using thermodilution techniques or clinically inferred. Conversely, four patients with myocardial infarctions with predominantly left ventricular failure and normal CVP, and two patients with pulmonary embolus with high CVP showed little change in mean shunt fraction. One myocardial infarction patient with left ventricular failure and high CVP became rapidly worse on HFJV with an abrupt fall in CVP from 18 mmHg to 8 mmHg and an acute rise in pulmonary wedge pressure (PWP) from 21 mmHg to 29 mmHg. Application of positive end-expiratory pressure (PEEP) 1.0 kPa reversed this.

IPPV resistant hypoxaemia. Of 36 patients with acute respiratory failure in whom the P_{aO_2} was inadequate (< 10 kPa on 100% oxygen plus PEEP) during IPPV, 29 had adequate P_{aO_2} (> 10 kPa) after 2 hours of HFJV. Twenty four of these 29 were subsequently weaned from HFJV to spontaneous ventilation. In contrast all seven patients in whom HFJV did not produce adequate oxygenation subsequently died of their presenting pathology.

Oxygen toxicity. Forty eight patients received $F_{iO_2} > 0.85$ for prolonged periods, the mean was 4.4 days (range 0.9–12). There was no clinical, radiological, bronchoscopic or, in the case of 12 of the 17 deaths for which

Table 3. Change in mean shunt with HFJV, expressed as percentage of cardiac output for the nine patients in whom shunt fell by more than 20%.

Diagnosis	Numbers	Pre-HFJV (range)	HFJV (range)
Cor pulmonale	3	32% (24–36%)	8% (4–16%)
Myocardial infarction	3	34% (29–41%)	11% (8–19%)
Pancreatitis	2	37% (26–48%)	11% (6–16%)
Pulmonary embolus	1	56% —	32% —

Table 4. Effect of changing delivery system on gas exchange. Results of arterial blood gas analyses in five patients following transfer from jet via tracheal tube to jet via minitracheostomy. Frequency, driving pressure, minute volume and F_{IO_2} were kept constant within each patient.

Patient	Jet tracheal tube		Jet minitracheostomy	
	P_{aCO_2} (kPa)	P_{aO_2} (kPa)	P_{aCO_2} (kPa)	P_{aO_2} (kPa)
1	4.6	18.2	5.7	16.7
2	4.9	21.6	5.9	18.2
3	4.4	19.7	5.5	16.3
4	4.8	24.2	5.7	19.6
5	5.2	16.3	6.3	14.7

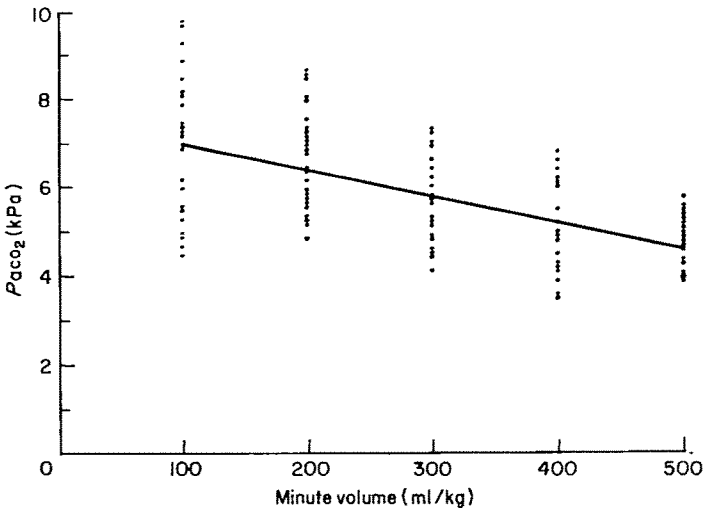


Fig. 3. Relationship between minute volume and P_{aCO_2} at constant ventilation frequency. Slope, $-6.726 \text{ E-}3$; intercept, 7.59; regression coefficient, -0.6546 ; $n = 164$, $p < 0.001$.

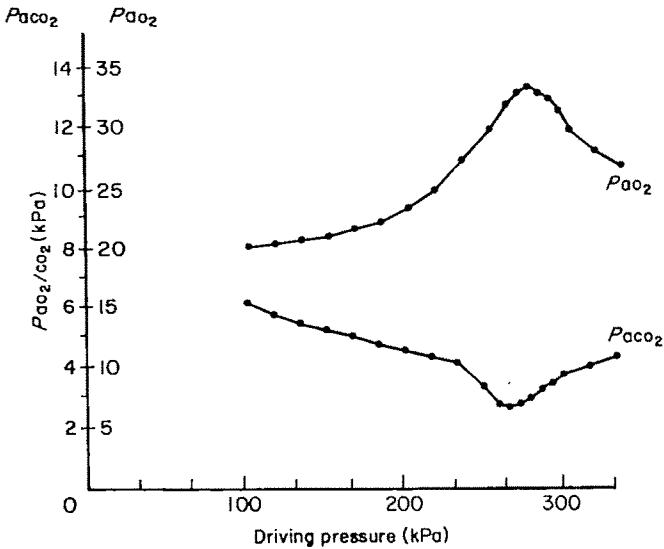


Fig. 4. Relationship between driving pressure used and arterial blood gas tensions at constant minute volume and frequency.

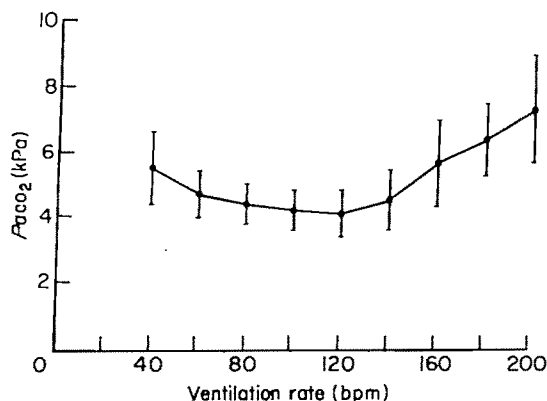


Fig. 5. Relationship between ventilation frequency and P_{aCO_2} at constant minute volume (pooled data for 18 patients).

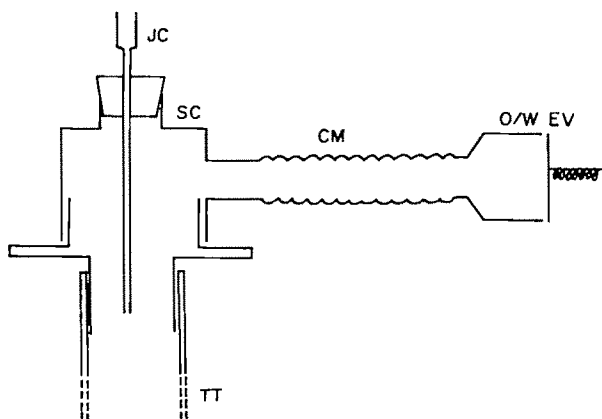


Fig. 6. Delivery system used to study the effects of varying cannula size. JC, jet cannula; SC, swivel connector; CM, catheter mount; O/W EV, one-way expiratory valve; TT, tracheal tube.

postmortem studies were available, histological evidence of pulmonary oxygen toxicity in any case. One 23-year-old male patient with bilateral chest trauma received an $F_{IO_2} > 0.85$ for 14 days and an F_{IO_2} of 0.75 for a further 8 days. He subsequently made a full recovery and showed no respiratory function test or chest X ray evidence of significantly impaired lung function. He complained of no respiratory symptoms at the time of discharge some 14 weeks after admission.

Carbon dioxide elimination. Fifty seven of the 63 patients achieved adequate CO_2 elimination ($P_{aCO_2} < 6.5$ kPa) during HFJV. It is noteworthy that of the six patients in whom CO_2 retention was a problem, two were admitted with severe status asthmaticus, three had severe bronchospasm in association with pulmonary infection and one had extensive bilateral pneumonic consolidation with a pulmonary compliance of < 50 ml/kPa. All six had shown marked CO_2 retention during IPPV.

Prediction of arterial carbon dioxide tensions. The influence of ventilation variables such as tidal and minute volumes, rate and driving pressure on arterial carbon dioxide tensions were studied after ethical approval. There was a significant correlation between P_{aCO_2} and minute volume in the 57 patients in whom normocapnia was achieved, as shown in Fig. 3. Arterial CO_2 tensions were also related to driving pressure used, the delivery system employed and the frequency of ventilation, as shown in Figs 4 and 5 and Table 4.

Driving pressure. The relationship of driving pressure to P_{aCO_2} at constant minute volume is shown in Fig. 4. (Minute volume was maintained at a constant level by

Table 5. Effect of varying cannula size on arterial blood gases for a single patient. Drive pressure, frequency, inspiratory time and F_{IO_2} were all constant; measurements were performed after 30 minutes in each case.

Cannula size (gauge)	P_{aCO_2} (kPa)	P_{aO_2} (kPa)
18	6.8	13.6
16	6.1	15.2
14	4.7	18.7
12	5.1	17.3
10	5.8	15.9

progressive reduction of the inspiratory time as driving pressure was increased). This curve was drawn from data obtained from one patient with cor pulmonale shortly before weaning from jet ventilation was commenced. His compliance at this time was relatively normal at 400 ml/kPa. HFJV was delivered via the tracheal tube system, without air entrainment. Qualitatively similar results were recorded in all seven patients in whom this effect was specifically studied. The peak and trough for O_2 and CO_2 tensions respectively are still unexplained but may be related to airway resonance.¹²

Influence of jet cannula size. The delivery system shown in Fig. 6 was used to study this effect in one patient. The radius of the cannula used during jet ventilation may have a profound effect upon the arterial CO_2 and O_2 tensions as illustrated in Table 5. The radius of the cannula will affect gas velocities within the trachea and bronchi which may explain the effect of different cannula sizes, or alternatively airway resonance may again contribute to this effect.¹² Carbon dioxide elimination, therefore, appears to be a complicated interaction between driving pressure, frequency, minute volume and patient delivery system, with a lesser dependence upon tidal volume and frequency than during conventional IPPV.

Optimal frequency of ventilation. Optimal frequency of ventilation as judged by blood gas analyses, cardiovascular pressure measurements and cardiac output determination varied from 80 bpm (1.3Hz) to 180 bpm (3Hz). In general, patients with poor compliance but stable cardiovascular parameters did better with slower rates (80–120 bpm, 1.3–2Hz) whilst patients with adequate pulmonary compliance and those with unstable cardiovascular parameters fared better at higher respiratory frequencies.

Cardiovascular function. Nineteen patients in the series had flow-directed pulmonary artery catheters inserted for assessment of their cardiovascular status. The comparative results for IPPV and after 3 hours HFJV are illustrated in Table 6. HFJV was adjusted to produce a P_{aCO_2} comparable to that during IPPV. The improvement in cardiac output, right atrial pressure, pulmonary artery pressure and mean arterial pressures are all significant. In addition, the use of dopamine in the two groups was not comparable. In the IPPV group the mean dosage of dopamine was 12 μ g/kg (7.3–16 μ g/kg/minute) compared with 5.3 μ g/kg (2.7–8.1 μ g/kg/minute) in the HFJV group, for the 13 patients in whom this agent was used. This also was statistically significant ($p < 0.05$).

Arteriovenous oxygen content difference. Twenty of 23 patients studied showed reduced arteriovenous saturation from a mean of 43% to 28%, which represented an arteriovenous oxygen content difference from a mean of 6.36 ml to 4.12 ml. Measurements were made at comparable arterial carbon dioxide tensions. Three patients showed no significant change (two myocardial infarctions, one pulmonary embolus).

Heart rate and systemic arterial pressure. For the series as a whole, heart rate fell by a mean of 18% (+ 6 to

Table 6. Comparison of cardiovascular parameters of 19 patients for IPPV and HFJV—for similar P_{aCO_2} . All pressure values are quoted as mean (range) mmHg.

Cardiovascular measurement	IPPV	HFJV	Significance
Cardiac output litres/minute	3.8 (2.6–4.8)	4.7 (3.4–6.3)	$p < 0.01$
Right atrial pressure	14 (2–24)	8 (–1–13)	$p < 0.05$
Pulmonary artery pressure	28 (19–47)	19 (12–33)	$p < 0.05$
Pulmonary wedge pressure	14 (10–21)	12 (9–17)	NS
Mean arterial pressure	84 (46–102)	93 (61–123)	$p < 0.05$

Table 7. Mean bronchial oesophageal and intrapleural pressures during HFJV and IPPV, without added PEEP. Pressures quoted in mmHg (range).

Site of measurement	IPPV		HFJV	
	Peak	Mean	Peak	Mean
Bronchial	28 (17–62)	11 (9–17)	16 (11–26)	9 (4–11)
Oesophageal	13 (9–21)	6 (3–11)	5 (2–9)	2 (–1–4)
Chest drain*	19 (15–31)	5 (3–10)	5 (3–12)	2 (–1–4)

*Chest drain clamped distal to point of measurement. No active air leak at time of measurement.

– 31%) whilst mean arterial pressure increased from a mean of 78 mmHg (46–118) to a mean of 91 mmHg (61–131) after transfer to HFJV.

Urine output. In 21 patients studied, urine output over a 6-hour period immediately before initiation of HFJV was compared with the 6-hour period immediately after initiation of HFJV. In the pre-HFJV period, the mean urine output was 38 ml/hour. This increased to a mean of 121 ml/hour in the 6-hour period following commencement of HFJV. This increased urine output occurred despite a net reduction in dopamine infusion from a mean of 9.3 $\mu\text{g/kg/minute}$ to 4.7 $\mu\text{g/kg/minute}$ in nine patients in whom this agent was used, and without significant change in diuretic usage.

Sodium excretion. Sodium excretion was studied in four patients before and after initiation of HFJV. All four showed a significant increase in urinary sodium excretion from a mean of 2.3 mmol/hour to 12.8 mmol/hour over the 6-hour period following initiation of HFJV. This was associated with an increased production of urine volume from a mean of 33 ml/hour to 116 ml/hour and represents an increase in urinary sodium concentration from 69.7 mmol/litre pre HFJV to 110.3 mmol/litre after HFJV.

Airway and intrathoracic pressures. Lower peak and mean airway pressures and lower alveolar pressures are amongst the advantages proposed for HFJV.⁵ Measurements were made of bronchial, oesophageal and intrapleural pressures (measured from chest drain catheters) in seven patients, with conventional vascular pressure transducers (Bentley Ltd) and a Kontron 108 monitor. Hard copy of the pressure waveforms obtained were used to derive true mean pressures against time for 30-second periods of measurement. The peak and mean pressures are shown in Table 7. Chest drain measurements were chosen as these represent the closest possible clinical method to determine normal intrapleural pressures. There was no clinically apparent air leak in any patient at the time of measurement; the chest drains were clamped immediately distal to the point of pressure sensing.

Bronchopleural leaks. Seven patients with large bronchopleural leaks were studied. During IPPV the mean leakage volume was > 500 ml/minute in all seven cases, 2.3 litres in one case. Within one hour of the initiation of HFJV, leaks stopped completely in five cases and decreased to approximately 50 ml/minute in the other two. Twenty four hours after the initiation of HFJV there was no detectable air leak in any patient whilst on HFJV.

PEEP effect of HFJV. The above pressure studies showed that during HFJV a significant PEEP effect was generated; airway pressures remained positive throughout the respiratory cycle by between 0.2 and 0.5 kPa at a respiratory rate of 120 bpm (2Hz). However, if the rate was reduced to below 100 bpm this PEEP effect was lost. PEEP was also lost if the inspiratory time was reduced to < 25% of total cycle time. Above 120 bpm, PEEP increased almost linearly with ventilation frequency, to levels in the order of 1.0–1.2 kPa at 180 bpm (3Hz) with an inspiratory time of 50%. It should be noted that where patients were capable of spontaneous respiratory effort, PEEP effect was lost during active inspiration by the patient, and airway pressures of –0.3 kPa were recorded on several occasions.

Effects of additional PEEP. PEEP (0.5–1.0 kPa) was added to 38 cases during HFJV. Its effects on arterial oxygen tensions were minimal and not clinically significant. Conversely, P_{aCO_2} fell in 32 cases when 0.5–1.0 kPa PEEP was added. In these cases the mean reduction of P_{aCO_2} was 0.8 kPa which was just significant at the 5% level. In general PEEP was well tolerated at lower frequencies (up to 140 bpm—2.3 Hz) but above this rate it generally produced significant decreases in blood pressure. This may have resulted from the combination of the PEEP effect generated during higher rate HFJV plus the added PEEP, which produced significant reduction in venous return.

Tracheobronchial toilet. HFJV can work as an open system, to permit ventilation to continue throughout the period of tracheal suction. We did not observe increased cyanosis, bradycardia or decreased arterial oxygen tensions in any patient during tracheal suction in this series. Conversely in two patients tracheal suction was deliberately continued for periods of 2 and 5 minutes via the tracheal tube. Arterial blood gases taken at one minute intervals showed no clinically significant changes in arterial oxygen tensions from presuction levels (see Table 8.)

Weaning from HFJV. This was achieved uneventfully on all 46 occasions where weaning from HFJV was attempted. Forty patients were weaned with the tracheal tube and six with the minitracheostomy. Weaning was performed by a progressive reduction of driving pressure, increase in ventilator rate to take advantage of the P_{aCO_2} frequency curve as in Fig. 5, or by a combination of both. Spontaneous ventilation occurred around the high frequency jet ventilation pulses in all cases, provided that the arterial CO_2 tensions were not depressed by ventilation. The criteria

Table 8. Arterial blood gas analyses for two patients during prolonged tracheal suction during HFJV.

Time (minutes)	Patient 1 (F _{IO} ₂ = 0.4)		Patient 2 (F _{IO} ₂ = 0.35)	
	PaCO ₂ (kPa)	PaO ₂ (kPa)	PaCO ₂ (kPa)	PaO ₂ (kPa)
0	4.8	22.3	5.2	18.7
1	4.6	20.7	4.8	16.9
2	4.5	19.3	4.6	16.3
3	—	—	4.5	15.8
4	—	—	4.7	15.6
5	—	—	4.6	15.1

chosen for weaning to commence were shunt below 15%, stable cardiovascular dynamics, and resolution of the pathology which precipitated acute respiratory failure. Weaning was generally achieved in less than 24 hours (85% of all cases, 39 patients) and in all cases in less than 48 hours.

Miscellaneous observations. In general we found the technique remarkably well tolerated, both by patients and by medical and nursing staff. Long term HFJV was both practicable and effective and made no greater demands on medical and nursing staff in terms of time or expertise than conventional mechanical ventilation. The sedation requirements of patients during HFJV appeared to be less than during IPPV although this was not formally studied.⁶ None of the patients in this series required the use of muscle relaxants in order to tolerate HFJV, while seven required their use to permit IPPV to be performed effectively.

Adverse effects of HFJV. No significant adverse effects peculiar to HFJV were observed in this series. There were no cases of iatrogenic air leak while on HFJV compared with seven cases whilst on IPPV. Indeed all seven showed a significant reduction in the size of air leak when transferred to HFJV. There were no mechanical or technical problems with the ventilation or delivery systems, nor was there any clinical, bronchoscopic or histological evidence of inadequate humidification in any case.

Discussion

The putative advantages of HFJV include improved cardiovascular stability,⁴ reduced airway pressures for similar gaseous exchange,⁵ greater preservation of renal function,² and reduced sedation requirements,⁶ all of which make the technique attractive to intensive care clinicians. Reports which cover the use of high frequency techniques in intensive care are, however, very limited and are mostly confined to anecdotal cases.^{13,14} This series includes a wide variety of pathologies with periods of HFJV of up to 24 days, and supports many of the claims made for HFJV.

The cardiovascular system. The significant improvement in cardiac output, right atrial pressure, pulmonary artery pressure and mean arterial pressures illustrated in Table 4 are similar to the effects reported by other workers in comparable patients¹⁵ and animal models.¹⁶ The significant reduction in shunt fraction after initiation of HFJV is also broadly similar to that reported by other workers.¹⁵

It is noteworthy that in the nine cases where HFJV produced a reduction in mean shunt of 20% or more, all nine had shown evidence of impaired right ventricular function and reduced cardiac output. We believe that this improvement resulted from a reduction in intrapulmonary pressure and pulmonary vascular resistance and therefore, right ventricular afterload, coupled with reduced intrathoracic pressures leading to improved venous return and a consequent increase in cardiac output. In four of the nine patients for whom determination was available, cardiac output increased by a mean of 23% (14–29%). All four showed reductions in pulmonary artery pressure which,

although not statistically significant, as cardiac output had increased significantly it can be inferred that pulmonary vascular resistance must have decreased after transfer from IPPV to HFJV.

High central venous pressure. The rapid transfer from IPPV to HFJV in a patient with a high CVP due to excessive preloading of the venous system, may result in abrupt increases in pulmonary wedge pressure and consequent decrease in cardiac output. This effect was observed on four occasions. The same situation is occasionally encountered in weaning when IPPV is interposed with periods of spontaneous respiration, or during intermittent mandatory ventilation weaning techniques. Removal of an elevated intrathoracic and intrapulmonary pressure may lead to an acute increase in right ventricular output. This in turn may lead to excessive preloading of the left side of the heart, with acute left ventricular failure, particularly in a compromised left ventricle.^{17,18}

On each of the four occasions when this effect was observed, the situation was corrected by adding PEEP 1.0 kPa to HFJV in an attempt to reverse this effect. We consider that excessive cardiac preloading is to be avoided if transfer to HFJV is required, although the use of PEEP may minimise the effects of a high preload to allow time for correction to a more appropriate level. PEEP can then be reduced gradually as this correction is achieved.

Adequacy of oxygenation. Adequate oxygenation was produced in all but seven patients and it is of considerable interest that in 36 patients with inadequate oxygenation during IPPV, despite the use of 100% oxygen plus PEEP, adequate oxygenation followed the introduction of HFJV. HFJV should therefore be considered in cases of IPPV-resistant hypoxaemia.

Oxygen toxicity. The unexpected absence of pulmonary oxygen toxicity in any patient in this series has been reported elsewhere.¹⁹ There is, however, a small amount of experimental evidence which suggests that the development of histological lesions of the type often attributed to pulmonary oxygen toxicity are seen less frequently during high frequency ventilation than during conventional mechanical ventilation.^{20–24}

Carbon dioxide elimination. Adequate carbon dioxide elimination was achieved in all but six patients. It is significant that five had severe bronchospasm and although all five had adequate oxygenation, the reduction in efficiency of carbon dioxide elimination was disappointing, as it is this category of patient who is most likely to develop pulmonary barotrauma complications whilst on IPPV. Nevertheless, the reduced airway pressures found during HFJV may still be an indication for HFJV in this type of patient.

Relationship of arterial carbon dioxide to ventilation parameters. The relationship of PaCO₂ to minute volume ventilation as shown in Fig. 4 is broadly similar to the findings of other workers.¹⁴ The relationship between driving pressure and arterial gas tensions of oxygen and carbon dioxide at constant minute volume (Fig. 5) has not been reported before. This type of response may, however,

have been witnessed inadvertently by Carlon and his co-workers: a patient with bronchopleural fistula showed an increase in PaO_2 from 6.6 kPa to 15.2 kPa when driving pressure during HFJV was reduced from 300 kPa to 240 kPa.¹³ The cause of this effect is unknown but may be related to audio frequency resonance within the airways during HFJV.¹²

Airway and intrathoracic pressures during HFJV. The relatively low airway pressures found during HFJV (Table 4) are similar to those reported by other workers.^{5,25,26} The pressures recorded from the chest drain catheters are also of interest as the closest possible reflection of true intrathoracic pressure. The close correlation between mean chest drain and oesophageal pressures is noteworthy and would suggest that mean oesophageal pressures are an accurate index of intrathoracic pressures during HFJV. It is perhaps not surprising that air leakage from bronchopleural fistulae was reduced so markedly in the patients in this series given these reduced airway pressures, particularly in the case of peak airway pressure. HFJV may therefore be the method of choice for mechanical ventilation of the lungs in patients with major air leak, and possibly in those at risk of developing such a leak.

PEEP effect. The production of 'auto PEEP' has already been described and has been reported by others.²⁷ It has been claimed that this PEEP effect may prevent aspiration of pharyngeal contents.²⁸ However, this effect is lost at ventilation frequencies below 100/minute and with short inspiratory time periods. In addition a voluntary inspiration by the patient may still produce a subatmospheric pressure within the trachea which would lead to tracheal soiling. HFJV alone cannot be relied upon to prevent aspiration.

Tracheobronchial toilet. The ability to perform prolonged tracheal toilet during HFJV was considered to be of benefit in several in this series with excessive sputum production, and in those with severely limited pulmonary reserve.

Weaning from HFJV. All three authors considered clinically that weaning was achieved more easily from HFJV than we were formerly used to with IPPV, although clearly this remains a subjective opinion. In this connexion special mention should be made of the jet minitracheostomy tube. In the six cases in which this was used as part of the weaning process, weaning was achieved with far greater ease than any other method in our experience. All six were alert and cooperative throughout weaning and even speech (albeit stertorous) was possible. Further trials of the minitracheostomy system are in progress and will be reported in due course, but initial results were most promising.

Renal function. The improvement in renal function after HFJV is of considerable interest and has been reported by others.⁴ Urinary excretion of water and electrolytes is a complex phenomenon influenced by many factors. Conventional IPPV may affect adversely urine output by its cardiovascular and hormonal effects. These may come directly or indirectly, as a result of its influence on intrathoracic pressure. Many studies have shown, including this one, that intrathoracic pressures during HFJV may be significantly lower than during IPPV,^{1,4,25} so it is not surprising that urine production and sodium excretion may be increased after transfer to HFJV. Fluid and sodium retention are common problems in ventilated patients and in general are of limited clinical significance. However, in patients with pre-existing excessive fluid loading, the use of HFJV in preference to IPPV would seem logical.

Technical considerations. The high minute volume capability of the ventilator enabled us to dispense with cumbersome and unpredictable entrainment systems to

augment tidal and minute volumes. Entrainment systems for the provision of humidification could also be dispensed with because the ventilator includes an efficient humidifier module.¹⁹ Patient interfacing is greatly simplified as a result which makes the technique of HFJV a more practicable proposition for long-term use. The alarm and fail-safe systems incorporated in the ventilator performed faultlessly in this study, even under deliberately simulated alarm conditions. The dangers of inadequate humidification during HFJV are well known and include mucociliary transport disruption,²⁹ mucosal epithelial damage, pulmonary inflammation and tissue necrosis.³⁰ There was no evidence of inadequate humidification in any case in this series. The technical difficulties of providing humidification during HFJV have been discussed elsewhere.⁹

Delivery systems. The dimensions and configurations of the delivery systems may have a profound effect upon clinical results as shown in Table 5. Further, in those situations where entrainment may occur (minitracheostomy, DTP techniques, open systems) the entrainment fraction can vary considerably from one system to another due to the design of the patient interface. Similarly, interpretation of the results obtained by different workers for intrathoracic and airway pressures during HFJV is complicated by the lack of uniformity in the position of the pressure-sensing catheter, both within the airway and in relation to the jet delivery point. This is not only clinically irritating but prevents direct comparison of the results of different workers in the field of HFJV, unless all the design variables are specifically stated or standardised.

Conclusion

The primary role of any system of mechanical ventilation is to maintain adequate oxygenation and carbon dioxide elimination until therapy and the natural reparative processes of the body alleviate the respiratory insufficiency. The clinician must often accept a compromise between less than ideal arterial blood gas results and the prevention of ventilation-related compromise of other organ systems. In short, mechanical ventilation should produce adequate gas exchange at minimal cost.

Viewed in this context we believe HFJV, as illustrated by the findings in this series, represents a significant step forward in the ventilatory management of acutely ill patients. The technique of prolonged HFJV appears both feasible and practicable. We disagree with Gallagher, Klain and Carlon³¹ that HFJV is not ready yet for routine clinical use, and support the contrary view expressed by Sladen and his co-workers¹⁴ that HFJV has come of age as a legitimate therapeutic modality in critical care medicine.

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References

1. BABINSKI M, KLAIN M, SMITH RB. High frequency jet ventilation. *American Society of Anesthesiologists Annual Meeting*. New Orleans, Louisiana, October 15-19, 1977; 781 (Abstract).
2. DRAZEN JM, KAMM RD, SLUTSKY AS. High frequency jet ventilation. *Physiological Reviews* 1984; **64** (2): 505-43.
3. SAAN AF, ROSSING TH, DRAZEN JM. Physiological bases for new approaches to mechanical ventilation. *Annual Review of Medicine* 1984; **35**: 165-74.
4. OBERG PA, SJOSTRAND U. Studies of Blood Pressure Regulation I. Common carotid artery clamping in studies of the carotid sinus baroreceptor control of the systemic blood pressure. *Acta Physiologica Scandinavica* 1969; **75**: 276-86.
5. KOLTON M, CATHAN CB, KENT G, VOLGYESI G, FROESE AB, BRYAN AC. Oxygenation during high frequency ventilation compared with mechanical ventilation in two models of lung injury. *Anesthesia Analysis Cleveland* 1982; **61**: 323-32.
6. KLAIN M, KESZLER H, FINE J. Intraoperative and postoperative use of high frequency jet ventilation. In: ARLINGTON VA. *Proceedings: AAMI 16th Annual Meeting, Short Papers on the New Dimension in Health Care*. Association for the Advancement of Medical Instrumentation, 1981 (Abstract).
7. SCHWARTZ L, KALLA RL, KLAIN M. Psychiatric response pattern to conventional ventilation compared to HFJV. *Critical Care Medicine* 1980; **8**: 243-7.
8. KLAIN M, SMITH RB. High frequency percutaneous trans-laryngeal jet ventilation. *Critical Care Medicine* 1977; **5**: 280-3.
9. SMITH BE. The Penlon Bromsgrove high frequency jet ventilator. A solution to the problems of humidification. *Anaesthesia* 1985; **40**: 790-6.
10. COMROE JH, FORSTER RE, DUBRIS AB, BRISCOE WA, CARLSEN E. *The lung. Clinical physiology and pulmonary function tests*, 2nd edn. Chicago: Year Book Medical Publishers, 1962.
11. NUNN JF. *Applied Respiratory Physiology*, 2nd edn. London: Butterworths, 1977.
12. SMITH BE. The role of acoustic resonance in high frequency ventilation. *British Journal of Anaesthesia* 1986; **58**: 130-1.
13. CARLON GC, COLE RB, KLAIN M, MCCORMACK PM. High frequency positive pressure ventilation in management of a patient with bronchopleural fistula. *Anesthesiology* 1980; **52**: 160-2.
14. SLADEN A, GUNTAPALLI K, MARQUEZ J, KLAIN M. High frequency jet ventilation in the postoperative period: a review of 100 patients. *Critical Care Medicine* 1984; **12**(9): 782-7.
15. CARLON GC, KAHN RC, HOWLAND RS, TURNBULL AD. Clinical experience with high frequency ventilation. *Critical Care Medicine* 1981; **9**: 1.
16. OTTO CW, CALKINS JM, QUAN SF, CONAHAN TJ, WATERSON CK, HAMEROFF SR. Cardiovascular consequences of high frequency ventilation. In: SHECK PA, SJOSTRAND UH, SMITH RB, eds. *Perspectives in high frequency ventilation*. Boston: Martinus Wijnhoff, 1983: 115-21.
17. BEACH T, MILLEN E, GRENISK A. Hemodynamic response to discontinuance of mechanical ventilation. *Critical Care Medicine* 1973; **1**: 85-90.
18. MATHRU M, RAP TLK, EL-ETR A, PIFFARE R. Haemodynamic response to changes in ventilatory patterns in patients with normal and poor left ventricular reserve. *Critical Care Medicine* 1982; **10**: 423-6.
19. SMITH BE, SCOTT PV, FISCHER HBJ, JOHNSTON P. Absence of pulmonary oxygen toxicity in association with high frequency jet ventilation. *Lancet* 1984; **1**: 505.
20. HAMILTON PP, ONAYEMI A, SMYTH JA, GILLEN JE, CUTZ E, FROESE AB, BRYAN AC. Comparison of conventional and high frequency ventilation: oxygenation and lung pathology. *Journal of Applied Physiology: Environmental Exercise Physiology* 1983; **55**: 131-8.
21. FEY DJM, BELLER U, EIERMANN T, LESCH R, DEITMAN M. Prolonged jet ventilation with high frequency injection. *Excerpta Medica* 1980; **533**: 248-54.
22. SMITH RB, CUTALE F, HOFF BH, BABINSKI M, GALINEAU J. Long term transtracheal high frequency ventilation in dogs. *Critical Care Medicine* 1981; **9**: 311-4.
23. KESZLER M, KLAIN R, MCCLELLAN L, NELSON D, PLATT M. Effects of conventional ventilation and high frequency jet ventilation on lung parenchyma. *Critical Care Medicine* 1982; **10**: 514-6.
24. FRANK I, NOACK W, LUNKENHEIMER PP, ISING H, KELLER H. Light and electron microscopic investigation of pulmonary tissue after high frequency positive pressure ventilation. *Anesthetist* 1975; **24**: 171-6.
25. CARLO W, CHATBURN R, MARTIN R. Decrease in airway pressure during high frequency jet ventilation in infants with respiratory distress syndrome. *Journal of Pediatrics* 1984; **104**: 101-7.
26. SLADEN A, GUNTAPALLI K, KLAIN M. High frequency jet ventilation versus intermittent positive pressure ventilation. *Critical Care Medicine* 1984; **12**(9): 788-90.
27. BEAMER WC, PROUGH DS, ROYSTER RL, JOHNSTON WE, JOHNSON JC. High frequency jet ventilation produces auto-PEEP. *Critical Care Medicine* 1984; **12**(b): 734-7.
28. KLAIN M, KESZLER H, BRADER E. High frequency jet ventilation in CPR. *Critical Care Medicine* 1981; **9**: 421.
29. NORDIN V, KEZLER H, KLAIN M. How does high frequency jet ventilation affect the mucociliary transport? *Critical Care Medicine* 1981; **9**: 160.
30. OPHOVEN JP, MAMMEL MC, GORDON MJ, BOROS SJ. Tracheo-bronchial histopathology associated with high frequency jet ventilation. *Critical Care Medicine* 1984; **12**(9): 829-32.
31. GALLAGHER TS, KLAIN M, CARLON G. Present status of high frequency ventilation. *Critical Care Medicine* 1982; **10**: 423-6.

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Anaphylactic reaction to isoflurane

Hypersensitivity reactions to halothane seem to be extremely rare with the possible exception of hepatitis, the mechanism of which is still unclear. We are aware of only one case of angioedema and rash to halothane¹ but none to the related agents enflurane or isoflurane. We report on a patient who developed an anaphylactic-like reaction to isoflurane.

A 7-year-old girl was scheduled for the insertion of grommets for transmeatal middle ear drainage in December 1986. She was healthy and did not use any drugs. She had had the same operation in November 1985 on which occasion she had been premedicated with a liquid mixture of atropine, codeine and diazepam. Induction of anaesthesia at that time was with nitrous oxide–oxygen (60%–40%) and halothane, which was later changed to isoflurane.

This time, after the same premedication, she was again anaesthetised with nitrous oxide and halothane, which was changed to isoflurane 10 minutes later. A generalised erythematous rash appeared within 5 minutes of starting isoflurane, accompanied by bronchospasm and tachycardia. There were, however, no signs of shock or hypotension and the pulse was felt clearly. Isoflurane was immediately discontinued and the trachea was intubated. She was treated with the antihistamine clemastine 1 mg and prednisolone 12.5 mg intravenously. The skin reaction faded away and bronchospasm disappeared after 3–5 minutes. Anaesthesia was thereafter continued uneventfully with halothane.

This adverse effect was probably caused by isoflurane. Hypersensitivity reactions to nitrous oxide do not seem to

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occur.² Atropine may cause contact dermatitis to eye drops or ointment,³ but we are not aware of any anaphylactic reactions to this agent. Premedication was administered 2.5 hours before the adverse effect appeared and this is not compatible with atropine-induced anaphylaxis. Thus the adverse effect was probably caused by either halothane or isoflurane. Halothane was, however, used again without ill effects. Moreover the anaphylactic reaction was temporally related to the administration of isoflurane, which means that this agent was most likely responsible. Whether it concerned a real anaphylactic reaction or an anaphylactoid reaction is difficult to determine. Isoflurane had been used in this patient one year earlier without adverse effect, but possibly she had become sensitised to this anaesthetic agent during that period. On the other hand, isoflurane may be irritant to the respiratory tract and we do not exclude the possibility that this stress factor caused histamine release through a nonimmunological pathway.

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References

1. BODMAN R. Skin sensitivity to halothane vapour. *British Journal of Anaesthesia* 1979; 51: 1092.
2. DESCOTES J. General anesthetics and therapeutic gases. In: DUKES MNG. ed. *Meyler's side effects of drugs*, 10th edn. Amsterdam, New York, Oxford: Elsevier, 1984: 183-96.
3. POLAK BCP. Drugs used in ocular treatment. In: DUKES MNG, ed. *Meyler's side effects of drugs*, 10th edn. Amsterdam, New York, Oxford: Elsevier, 1984: 875-85.

The analgesic effects of ketamine

We were interested to read the report by Dr Owen and his colleagues (*Anaesthesia* 1987; 42: 1051-6) on morphine and ketamine infusions for postoperative analgesia. They demonstrated no analgesic effect from a ketamine infusion of 4 µg/kg/minute which produced a mean plasma concentration of 179 ng/ml (range 126-256 ng/ml). We also failed to find any analgesic effect after a 30-minute subanaesthetic infusion of ketamine at 1 mg/kg/hour despite a mean plasma level of 217 ng/ml (range 107-354 ng/ml) in a recent study, using the ischaemic tourniquet time test as described by Clements and Nimmo.¹

These results are surprising in view of the previous studies,¹⁻² which demonstrated significant elevation of pain threshold with plasma ketamine levels of 100 to 150 ng/ml. We can only agree with Owen and his co-workers with regard to the role of placebo effect in the previous studies, which were carried out on informed junior anaesthetists with saline as a control, which made it obvious when the active agent was being infused. Subjects in our study received a subanaesthetic infusion of either ketamine, methohexitone or propofol in a random sequence at weekly intervals to produce the same degree of sedation. Double-blinding was achieved by the concurrent administration of intralipid or saline as appropriate by an identical syringe pump.

A review of the evidence for ketamine analgesia is interesting. There is no doubt that in man ketamine produces a state of dissociative anaesthesia which allows painful procedures to be performed. Analgesia, however, implies a lack of response to noxious stimuli without concurrent depression of consciousness. Ketamine in animals is a poor or nonexistent analgesic in nonprimates, and produces somatic analgesia in primates in doses of 5-25 mg/kg intramuscularly, but only when the animal is in a state of cataleptoid stupor.³ The difference between the analgesic dose and disorienting dose in animals is less than 1 to 4 as compared to 160 for morphine.⁴

Many of the clinical reports on ketamine analgesia are anecdotal or poorly controlled. Doses of ketamine are often used that would be considered anaesthetic by most anaesthetists, or there is a failure to specify the method of assessment of analgesia, conscious level or degree of dissociation of the patient. Thus Caro,⁵ a casualty surgeon, gave 1-2 mg/kg of ketamine intravenously to patients for minor casualty-type procedures and, not surprisingly, found that it provided suitable analgesia. Corssen and Domino⁶ reported a series of 130 patients who underwent short sur-

gical procedures. Ketamine 1-2 mg/kg intravenously or 8-10 mg/kg intramuscularly, was given after an opiate premedication, and analgesia was adequate in most instances although some patients required nitrous oxide supplementation. They demonstrated analgesia only when the peculiar state of altered consciousness or dissociation was present.

Itō and Ichiyangi⁷ gave a bolus of 0.6 mg/kg intravenously of ketamine in the postoperative period followed by an infusion of 1.5 mg/kg/hour for analgesia after abdominal surgery and, perhaps not unexpectedly, found that most patients lay quiet and seemed to be asleep during the infusion; this infusion rate produces plasma levels associated with anaesthesia.⁸ Knox and his colleagues⁹ who used ketamine in short gynaecological procedures state 'considering that ketamine is classed as an analgesic it was surprising to find patients complaining of severe pain soon after operation'.

The analgesic effect is closely related to the dissociative state with subanaesthetic doses. Slogoff *et al.*¹⁰ used subanaesthetic doses of 1.5-2 mg/kg intramuscularly for burns treatment and found that this produced approximately 15 minutes of analgesia and 20 minutes of disorientation; the analgesia was heralded by nystagmus, psychic relaxation and blank affect.

We agree with Dr Owen and his colleagues that there is no evidence to support the recommendation that a low dose infusion of ketamine, to achieve a plasma concentration of 100-150 ng/ml, provides a significant analgesia. It may also be that the dissociative anaesthesia which ketamine produces in man is being falsely equated with analgesia and that it is time to reappraise critically the much quoted analgesic properties of ketamine.

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References

1. CLEMENTS JA, NIMMO WS. Pharmacokinetics and analgesic effect of ketamine in man. *British Journal of Anaesthesia* 1981; 53: 27-30.
2. GRANT, IS, NIMMO, WS, CLEMENTS JA. Pharmacokinetics and analgesic effects of i.m. and oral ketamine. *British Journal of Anaesthesia* 1981; 53: 805-9.

3. GREEN CJ, KNIGHT J, PRECIOUS S, SIMPKIN S. Ketamine alone and combined with diazepam or xylazine in laboratory animals: a 10-year experience. *Laboratory Animals* 1981; **15**: 163-70.
4. COLLIER HOJ, DINNEEN LC, JOHNSON CA, SCHNEIDER C. The abdominal constriction response and its suppression by analgesic drugs in the mouse. *British Journal of Pharmacology* 1968; **32**: 295-310.
5. CARO DB. Trial of ketamine in an accident and emergency department. *Anaesthesia* 1974; **29**: 227-9.
6. CORSSSEN G, DOMINO EF. Dissociative anaesthesia: further pharmacologic studies and first clinical experience with the phencyclidine derivative C1-581. *Anesthesia and Analgesia* 1966; **45**: 29-40.
7. ITO Y, ICHIYANAGI K. Postoperative pain relief with ketamine infusion. *Anesthesia* 1974; **29**: 222-6.
8. IDVALL J, AHLGREN I, ARONSEN KF, STENBERG P. Ketamine infusions, pharmacokinetics and clinical effects. *British Journal of Anaesthesia* 1979; **51**: 1167-73.
9. KNOX JWD, BOVILL JG, CLARKE RSJ, DUNDEE JW. Clinical studies of induction agents XXXVI: Ketamine. *British Journal of Anaesthesia* 1970; **42**: 875-85.
10. SLOGOFF S, ALLEN GW, WESSELS JV, CHENEY DH. Clinical experience with subanaesthetic ketamine. *Anesthesia and Analgesia* 1974; **53**: 354-8.

A reply

It is pleasing to see confirmation of our findings so soon after our work was published. Clearly intravenous ketamine in very low doses does not produce analgesia separate from anaesthesia. Ketamine has a definite place as an anaesthetic in our armamentarium. Small doses (0.5-2 mg/kg) do provide anaesthesia, although signs often used to establish induction of anaesthesia may be lacking. If anaesthesia is maintained with other agents for at least 45 minutes the concentration of ketamine in plasma is well below those seen on recovery from pure ketamine anaesthesia (around

600 ng/ml)^{1,2} and the adverse psychotomimetic effects associated with the immediate postketamine anaesthesia state and the related plasma concentrations can be avoided.

Ketamine is a racemic mixture of its optical isomers. The isomers have different activities and one is far superior as an analgesic anaesthetic.³ The vast majority of synthetic chiral drugs are presented as their racemates. These drugs are generally considered to be mixtures of relatively 'active' and 'inactive' isomers. However the 'inactive' isomer may not be passive bulk⁴ and can have sinister properties.⁵ There is a strong case that, when new anaesthetic drugs are developed, only one isomer is licensed.

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References

1. AUDIBERT GB, BULLA G, COSENTINO S, PALAZZO G, ROMANO G, ZAGAMI A. Concentrazione ematica di ketamina in fase di risveglio. *Minerva Anestesiologica* 1984; **50**: 55-7. (English title) Blood ketamine concentration in patients on arousal from anaesthesia.
2. IDVALL J, AHLGREN I, ARONSEN KF, STENBERG P. Ketamine infusions: pharmacokinetics and clinical effects. *British Journal of Anaesthesia* 1979; **51**: 1167-73.
3. WHITE PF, SCHÜTTLER J, SHAFER A, STANSKI DR, HORAI Y, TREVOR AJ. Comparative pharmacology of the ketamine isomers. Studies in volunteers. *British Journal of Anaesthesia* 1985; **57**: 197-203.
4. WILLIAMS K, LEE E. Importance of drug enantiomers in clinical pharmacology. *Drugs* 1985; **30**: 333-54.
5. CHAU TT, HARRIS LS. Comparative studies of the pharmacological effects of the d- and l- isomers of codeine. *Journal of Pharmacology and Experimental Therapeutics* 1980; **215**: 668-72.

Aminophylline and propofol: apparent antagonism

The nonspecific action of aminophylline which results in antagonism of the sedation caused by diazepam has been recognised before.¹⁻³ We wish to report the possibility of a similar interaction between aminophylline and propofol.

A 24-year-old girl who weighed 50 kg required respiratory support for 17 days on our intensive care unit for the treatment of status asthmaticus and persistent intense bronchospasm. She was treated with nebulised salbutamol, intravenous antibiotics and steroids, and infusions of terbutaline sulphate, ipratropium bromide, and aminophylline. The rate of aminophylline infusion was modified according to blood levels.

Sedation proved a difficult problem during her stay in intensive care. She frequently became agitated despite standard regimens of midazolam, lorazepam, phenoperidine and alfentanil in various combinations, and in view of this she was eventually treated by an infusion of propofol. This was effective, but the requirements were high, 400-500 mg/hour was necessary at times. We were interested to note that after discontinuation of aminophylline the infusion requirements of propofol apparently decreased. In a 12-hour period from 1900 hours on day 13, when used as the sole sedation agent she required a total of 6950 mg of propofol. In the same period 36 hours after withdrawal of aminophylline, on day 16, she required 3900 mg, although

the boluses of midazolam 2.5 mg were also administered. The only other change in medication had been a reduction in steroid dosage.

Part of the difficulty encountered in sedation with this patient may be attributed to the general cerebral excitatory effect produced by aminophylline when therapeutic levels are achieved. Nevertheless an antagonistic interaction with propofol sedation is possible, and has not to our knowledge been previously described.

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References

1. STIRT JA. Aminophylline is a diazepam antagonist. *Anesthesia and Analgesia* 1981; **60**: 767-8.
2. ARVIDSSON SB, EKSTROM-JODEL B, MARTINELL SAG, NIEMAND D. Aminophylline antagonises diazepam sedation. *Lancet* 1982; **ii**: 1467.
3. NIEMAND D, MARTINELL S, ARVIDSSON S, SVEDMYR N, EKSTROM-JODEL B. Aminophylline inhibition of diazepam sedation: is adenosine blockade of GABA-receptors the mechanism? *Lancet* 1984; **i**: 463-4.

Lupus anticoagulant—implications for the obstetric anaesthetist

The case report by Malinow and colleagues (*Anaesthesia* 1987; **42**: 1291-3) provides an interesting account of the lupus anticoagulant. Malinow describes the potential risk of regional anaesthesia in a patient on aspirin treatment,

but does not discuss some other potential hazards which face the anaesthetist involved in the care of a patient with systemic lupus erythematosus (SLE) and the lupus anticoagulant (LA).

Both arterial and venous thrombosis are described but 70% of thrombotic events occur in the venous system, the most common site is the leg veins. Thrombosis of pulmonary, hepatic, renal and retinal veins may also occur. From previous reports anticoagulant therapy with heparin or warfarin is effective prophylaxis against further episodes of venous thrombosis.¹⁻³ A high recurrence rate after withdrawal of oral anticoagulants subsequent to venous thrombosis in LA patients, has prompted the recommendation that all such patients should be on long term anticoagulant therapy once a deep vein thrombosis has been diagnosed.¹⁻³ Therefore it is likely, given the frequency of thrombotic events in patients with the LA and allowing for the high fetal loss, that women who receive anticoagulant therapy will present for delivery. Regional anaesthesia is contraindicated in such patients.

Treatment of arterial, including cerebral, thrombosis is complicated by the fact that there is little data on the efficacy of various antithrombotic regimens. Patients may be treated with anticoagulants, antiplatelet or immunosuppressive agents. In the absence of other coagulation abnormalities bleeding is rare, but the anaesthetist faced with a patient with a prolonged partial thromboplastin time may feel reluctant to perform regional anaesthesia. Unfortunately there is no data to guide the anaesthetist through this dilemma. Lechner¹ in a review of the literature points out the high association between fetal loss and thrombotic events which occur in connexion with pregnancy and following abortion or delivery. Therefore, pregnancy may increase the risk of thrombosis in these patients. Pregnancy has also been associated with exacerbations of disease in patients with SLE, although there is one report to the contrary. Since SLE is a multisystem disorder, exacerbations of cardiac, respiratory, renal or neurological disorders carry important implications for the anaesthetist involved in the care of these women.

Malinow reports, in reference to the pathophysiology, that the vascular production of prostacyclin is inhibited by

the LA. This is a very controversial finding with papers arguing for and against this hypothesis. French workers have found that the LA inhibits the activation of protein C, one of the body's natural anticoagulants.⁵ This mechanism for the increased thrombotic tendency is popular among European haematologists but it still does not explain the arterial thrombosis which is uncommon in protein C deficiency.

Pregnancy in a patient with SLE and the LA represents a considerable risk to both mother and fetus and is usually managed in a specialised centre. An increased incidence of Caesarean section was reported in patients with SLE⁶ and this probably applies equally, if not more so, to patients with the added complication of the lupus anticoagulant. Anaesthetists are very likely to be involved in the management of these patients.

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References

1. LECHNER K. Lupus anticoagulants and thrombosis. *Thrombosis and Haemostasis* 1987; **58**: 525-47.
2. MUEH JR, HERBST KD, RAPAPORT SI. Thrombosis in patients with the lupus anticoagulant. *Annals of Internal Medicine* 1980; **92**: 156-9.
3. ELIAS M, ELDOR A. Thromboembolism in patients with the 'lupus'-type circulating anticoagulant. *Archives of Internal Medicine* 1984; **144**: 510-5.
4. LOCKSHIN MD, REINITZ E, DRUZIN ML, MURRMAN M, ESTES D. Lupus pregnancy. Case-control prospective study demonstrating absence of lupus exacerbation during or after pregnancy. *American Journal of Medicine* 1984; **77**: 893-8.
5. FREYSSINET JM, CAZENAVE JP. Lupus-like anticoagulants, modulation of the protein C pathway and thrombosis. *Thrombosis and Haemostasis* 1987; **58**: 679-81.
6. TOZMAN ECS, UROWITZ MB, GLADMAN DD. Systemic lupus erythematosus and pregnancy. *Journal of Rheumatology* 1980; **7**: 624-32.

Palsy after femoral nerve block

The letter from Dr Freck (*Anaesthesia* 1988; **43**: 167-8) was very interesting.

He is correct to state that there are few published reports of severe, long-lasting nerve damage after femoral nerve block. It is generally recognised to be a safe block with occasional dysaesthesia as the main problem. However, the risks of damage to any nerve depend on the technique used, and it may be that Dr Freck has chosen an inappropriate technique for this block. He claims to use the method described by Smith;¹ however, this is a technique used for blocking the brachial plexus, and Smith advocated the use of short bevelled insulated needles for this. Dr Freck has used neither.

If nerve stimulators are used inappropriately² by the inexperienced, is there not a danger of damage resulting from an attempt to position the needle as close as possible to the nerve? There are indications for their use in certain circumstances, for example, the classical posterior approach to the sciatic nerve, or supraclavicular brachial plexus block, but under these conditions I recommend that a period of training is undergone before the solo attempt is made since competent use of a nerve stimulator is not easily acquired. Short bevelled insulated needles should be used.

Other blocks do not require the use of a nerve stimulator; one such is the anterior approach to the sciatic nerve³ and, I suggest, the femoral nerve block since the traditional method described in standard textbooks of local anaesthesia⁴ is safe, even in anaesthetised patients.⁵

Finally, may I add that there is now clear evidence that

uninsulated needles should not be used with nerve stimulators^{6,7} since the point of maximum current does not come from the needle tip but 0.5-1.0 cm proximal to it, so that the game of 'hunt the nerve' if played by the inexperienced, may result in the nerve being entered by the needle before maximum stimulation occurs.

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References

1. SMITH BE. Distribution of evoked paraesthesia and effectiveness of brachial plexus block. *Anaesthesia* 1986; **41**: 1112-5.
2. McNICOL LR. Quality of axillary brachial plexus block. *Anaesthesia* 1987; **42**: 774-5.
3. McNICOL LR. Anterior approach to sciatic nerve block in children: loss of resistance or nerve stimulator for identifying the neurovascular compartment. *Anesthesia and Analgesia* 1987; **66**: 1199 (letter).
4. ENGLESSON S. Nerve block in the region of the hip joint. In: ERIKSSON E. ed. *Illustrated handbook in local anaesthesia*. London: Lloyd-Luke, 1979.
5. McNICOL LR. Lower limb blocks for children. Lateral cutaneous and femoral nerve blocks for postoperative pain relief in paediatric practice. *Anaesthesia* 1986; **41**: 27-31.
6. BASHEIN G, HASCHKE RH, READY LB. Electrical nerve location: numerical and electrophoretic comparison of insulated vs uninsulated needles. *Anesthesia and Analgesia* 1984; **63**: 919-24.
7. FORD DJ, PITHER C, RAJ PP. Comparison of insulated and uninsulated needles for locating peripheral nerves with a peripheral nerve stimulator. *Anesthesia and Analgesia*. 1984; **63**: 925-8.

Estimating the train-of-four ratio: an inexpensive alternative

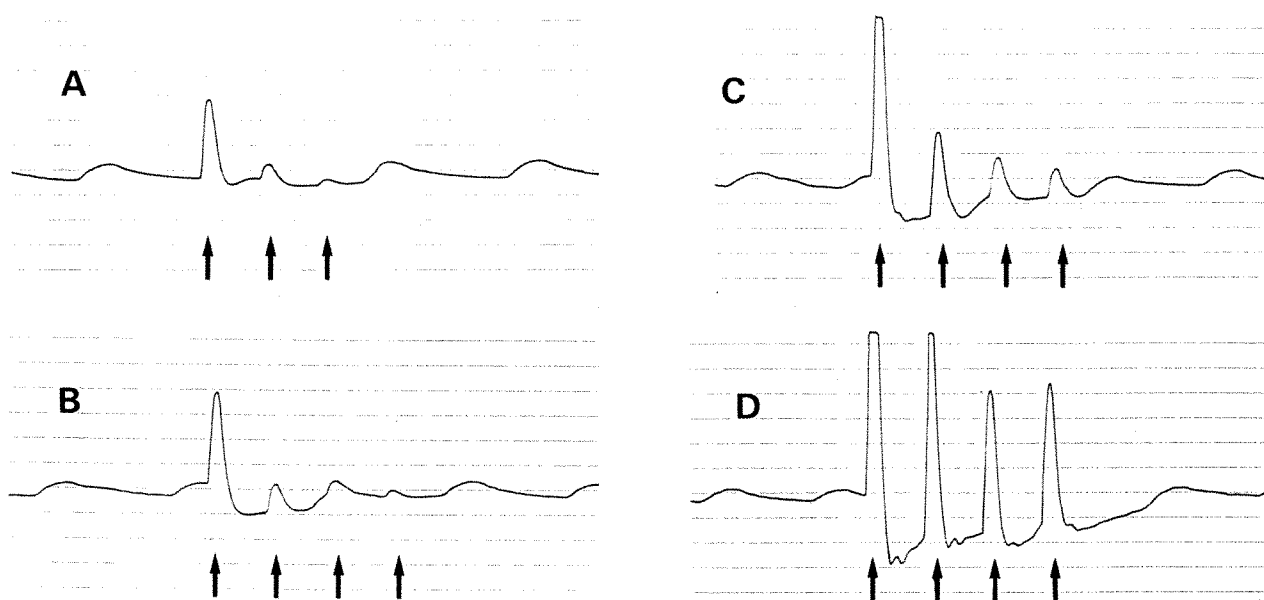


Fig. 1. Arrows indicate thumb movement after ulnar nerve stimulation.

Monitoring of the train-of-four (TOF) pattern of nerve stimulation is probably the most sensitive and reliable method to assess the degree of residual neuromuscular blockade.¹ However, estimation of the TOF ratio can be difficult by either sight or touch; to calculate the ratio, a permanent copy of the EMG is usually necessary and this requires more sophisticated and expensive equipment than a simple nerve stimulator.

If a standard pulse monitor (Simonsen and Weel pulse plethysmograph and recorder) is attached to the patient's thumb and, with reduction of the size of the pulse waveform on the display, the movement produced by ipsilateral ulnar nerve stimulation is superimposed on the pulse waveform and this enables a more reliable estimate of the TOF ratio to be made.

In A (Fig. 1), 15 minutes after a 10-mg increment of atracurium the first three twitches are seen with consider-

able fade; B shows all four twitches present, though fade persists; in C, one minute after intravenous neostigmine (2.5 mg) and atropine (1 mg), the TOF ratio (T₄/T₁) is greater than in B though still less than 50%. In D the TOF ratio is greater than 50%. The twitch peaks can be distinguished from the pulse peaks because the former do not produce an audible beep on the monitor.

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1. JONES RM. Neuromuscular transmission and its blockade. *Anaesthesia* 1985; **40**: 964-76.

Atraumatic nasopharyngeal intubation for upper airway obstruction

We report the case of a man who presented with upper airway obstruction because of angioedema of the tongue and the use of the Linder 'Bubble Tip' nasopharyngeal tube (Polamedco Inc.) to relieve this obstruction.

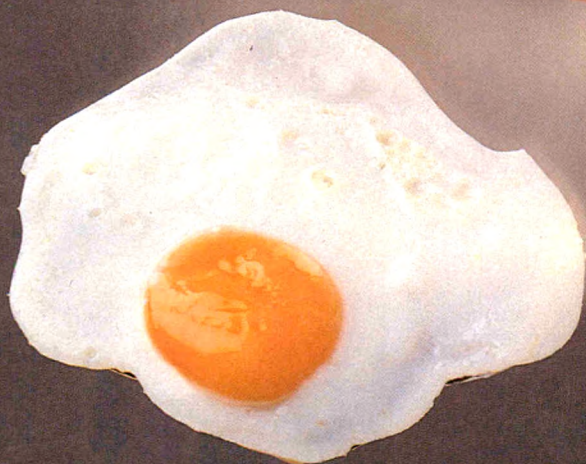
A 26-year-old Iranian man who weighed 120 kg, presented to casualty one morning with a 2-hour history of increasing difficulty in breathing, due to an acutely swollen tongue. He had no significant past medical history nor was there any particular causative factor. Immediate treatment in casualty included 40% oxygen by face mask, adrenaline 1 mg subcutaneously, hydrocortisone 200 mg intravenously, chlorpheniramine 10 mg intravenously, assuming the diagnosis of angioedema, cause unknown, but his condition rapidly deteriorated.

His tongue had swollen to occlude the oropharynx almost completely, including the nasopharynx from below and the larynx from above and caused upper airway obstruction. Immediate clearance of the airway was

essential. Location of the trachea and larynx for cricoid-thyroidotomy or tracheostomy was potentially very difficult and hazardous because of his bull neck and distress. It was decided to clear the airway with a nasopharyngeal tube pushed down past the oropharynx beyond the tongue. We needed to avoid trauma to the oedematous and friable nasal and oral mucosal membranes which could cause haemorrhage, and which would drown the patient if bleeding occurred below the tongue, since he would be unable to expectorate the blood adequately. The Lindner Nasopharyngeal tube with 'Bubble tip' introducer, (Figs 1 and 2) was therefore used. The nasal passages were sprayed with lignocaine spray 4% (total 160 mg) and after lubrication of the introducer and the tube with KY jelly, the introducer was positioned with the tip protruding only 1.0 cm, which restricted the inflation of the 'bubble tip' to the same external diameter of the tube, (Fig. 3). They were then gently inserted through the right nostril and advanced down

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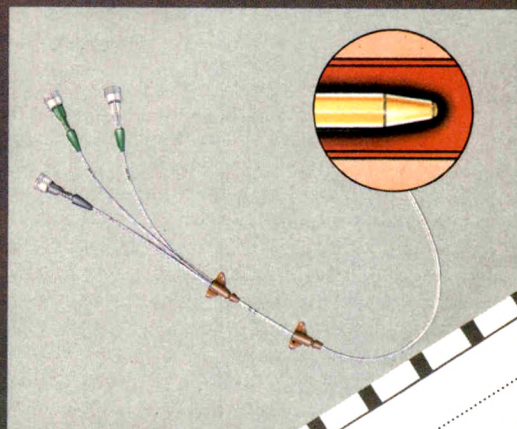
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3. Tetanus: 0.1-0.3mg diazepam/kg body weight by i.v. injection

and repeated every 1 to 4 hours as required. Alternatively, a continuous infusion of 3-10 mg/kg body weight every 24 hours may be used.

4. Anxiety and tension, acute muscle spasms, acute states of excitation, delirium tremens: The usual dose is 10mg repeated at intervals of 4 hours as required.

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CONTRA-INDICATIONS, WARNINGS, ETC. Concomitant use of central nervous system depressants, e.g. alcohol, general anaesthetics, narcotic analgesics or antidepressants, including MAOI's will result in accentuation of their effects. Treatment with diazepam may cause drowsiness and increase the patient's reaction time. This should be considered where alertness is required, e.g. driving a car. As with any benzodiazepine, excessive or prolonged use may result in the development of some psychological dependence with withdrawal symptoms on discontinuation. Use with caution in patients with impairment of

renal or hepatic function.

Pregnancy and Lactation: Diazepam crosses the placenta and should not be used during pregnancy unless considered essential. Large maternal doses administered during delivery may produce clinical effects in the newborn. Diazepam can be transmitted in breast milk and clinical effects may occur in the breast-fed infant.

Side effects: May rarely cause local pain or thrombophlebitis. Rare instances of a local painless erythematous rash around the site of injection. Urticaria and, rarely, anaphylaxis have been reported.

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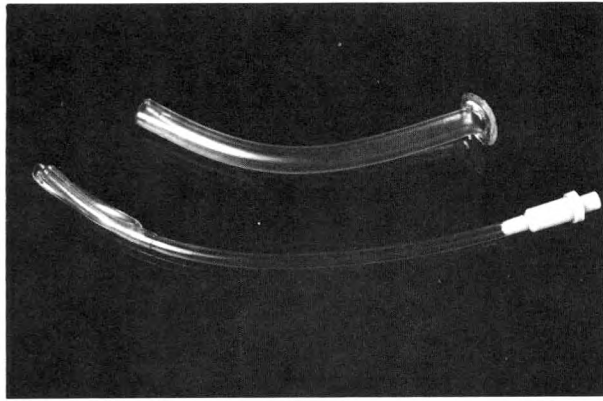


Fig. 1. Linder nasopharyngeal tube with separate bubble tip introducer deflated.

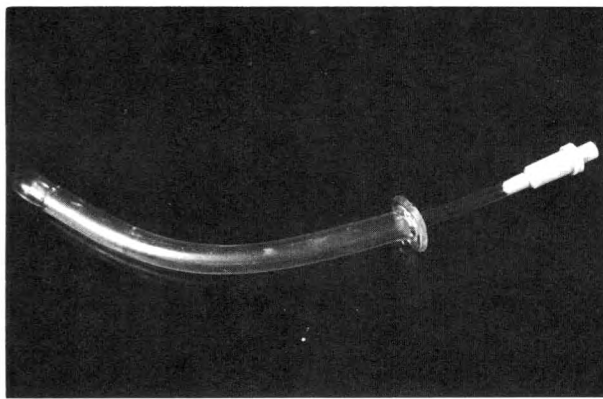


Fig. 2. The introducer in place and bubble tip inflated.

past the naso- and oropharynx. There was immediate relief of the obstruction as the introducer was withdrawn and no evidence of any haemorrhage or trauma to the mucosa. The passage of a soft-tipped suction catheter to remove clear secretions, confirmed that there was no haemorrhage. The patient achieved adequate ventilation through the 7.5 mm internal diameter airway and his general condition rapidly improved.

High frequency jet ventilation during bronchial surgery

This is a comment on the recent case report by McKinney *et al.* (*Anaesthesia* 1988; **43**: 25–6) which described the use of high frequency jet ventilation (HFJV) delivered by twin catheters during sleeve resection and major bronchial surgery. It would be premature to accept this technique as an improvement over that of ventilation by a double lumen bronchial tube, for sleeve resection of the right upper lobe; or the technique of placing tracheal tubes directly into the main bronchi, to facilitate ventilation during tracheal and carinal resection, as advocated by Geffin and colleagues.¹

In the case reported, the right lower lobe collapsed intra-operatively despite the use of HFJV. Relative hypoxia and hypercarbia ensued. The patient also developed hypercarbia and required mechanical ventilation in the post-operative period. The authors state that this was because of deterioration in the patient's pre-existing lung condition of chronic obstructive airways disease, although the chest X ray and arterial blood gas analysis were both within

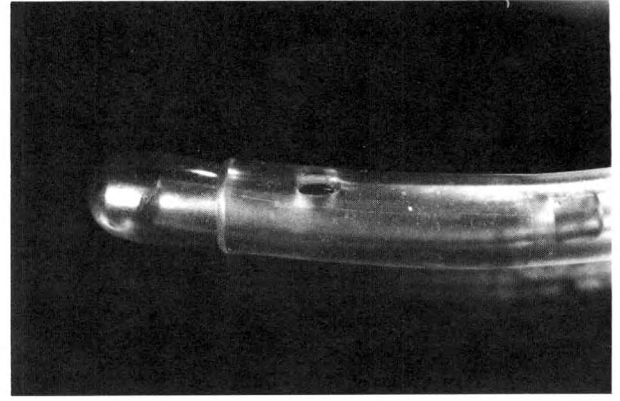


Fig. 3. Inflated bubble tip which protrudes 1.0 cm from the end of the tube; the external diameter is then the same as that of the tube itself.

Further hydrocortisone 200 mg and chlorpheniramine 10 mg were given and 6 hours after admission the swelling had subsided adequately to allow removal of the nasopharyngeal tube. The patient had a clear airway and could talk and swallow normally. Later investigation revealed the patient has a diagnosis of hereditary angioedema with C₁-esterase inhibitor deficiency, levels 0.006 mg/litre (0.16–0.26 mg/litre).^{1,2}

This individual case confirms the evidence of Casey,³ that the bubble tip nasopharyngeal tube allows atraumatic nasal intubation with minimal subsequent haemorrhage, features that were obviously life saving in this case.

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T.M.W. LONG

References

1. FRANK MM, GELFAND JA, ATKINSON JP. Hereditary angioedema: the clinical syndrome and its management. *Annals of Internal Medicine* 1976; **84**: 580–93.
2. HOPKINSON RB, SUTCLIFFE AJ. Hereditary angioneurotic oedema. *Anaesthesia* 1979; **34**: 183–6.
3. CASEY W. A new nasopharyngeal airway. *Care of the Critically Ill* 1986; **2**: 61.

normal limits before operation, and the pulmonary function tests were only slightly below predicted values.

The complications described by McKinney *et al.* during and after bronchoplastic surgery are well recognised, although the requirement for mechanical ventilation would be considered a major setback in most units. It is significant that the use of HFJV did not prevent the occurrence of these complications.

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J.W.W. GOTHARD

Reference

1. GEFFIN B, BLAND J, GRILLO HC. Anesthetic management of tracheal resection and reconstruction. *Anesthesia and Analgesia* 1969; **48**: 884–96.

A reply

Dr Gothard is quite correct when he writes that it would be premature to assume that the use of twin catheters in association with HFJV is an improvement in technique for tracheal carinal and bronchial surgery. Three patients only have presented for this type of surgery in our unit in the last 5 years. Thus, a considerable time will elapse before we can confidently claim an important advance. Nevertheless, on the basis of these three patients our surgeons would be most reluctant to revert back to the techniques defined by Geffin *et al.* almost 20 years ago.

The anaesthetic technique we described is simple, safe and effective. Surgical access is not restricted by the catheters in the same way as tracheal or bronchial tubes. The problems encountered in our case report (*Anaesthesia*

1988; 43: 25–26) have not occurred subsequently. Less enthusiastic retraction at that time by the surgical assistant would have prevented collapse of the lower lobe. Similarly, an awareness that the catheter can occlude the right upper lobe bronchus can be avoided by careful catheter placement.

It is unfair to attribute the requirement for postoperative ventilation on the intra-operative technique. A patient with chronic obstructive airway disease on long-term steroids and undergoing sleeve resection of the bronchus will always be a potential candidate for postoperative ventilatory support regardless of technique.

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D.L. COPPEL
J.R. GIBBONS

Suxamethonium for penetrating eye injuries

We note with interest the reports of Abbott and Samuel (*Anaesthesia* 1987; 42: 1008–12) and Mirakhur *et al.* (*Anaesthesia* 1987; 42: 944–9) about intra-ocular pressure (IOP) with early tracheal intubation using large doses of vecuronium.

We attempted to resolve this problem by investigating the use of pancuronium, a non-depolarizing neuromuscular agent with a relatively short onset time. Forty patients of ASA class 1 and 2 who presented for elective abdominal surgery were allocated to one of two groups in a double blind trial. Premedication was with lorazepam 1–3 mg. Induction was with thiopentone 4 mg/kg, and pancuronium 0.1 or 0.15 mg/kg was injected. The trachea was intubated at 90 seconds after the pancuronium. Neuromuscular blockade was monitored by stimulation of the ulnar nerve at the wrist with a standard train-of-four technique. Force of adduction was measured by strain gauge transducer to pen recorder.

The larger dose (0.15 mg/kg) was associated with a more rapid mean (SD) time to maximum twitch depression of 196.2 (63.2) seconds as against 240.0 (70.5) seconds for the 0.1 mg/kg dose ($p < 0.05$ Student's *t*-test). Intubating conditions were determined by the anaesthetist, who was unaware of the dose of pancuronium.

There was the minimal reaction to intubation in one out of 20 patients in the lower dose group and 10 out of 20 patients in the higher dose group (i.e. no straining or bucking). We did not measure IOP but in 50 percent of the higher dose group, the reaction to intubation was such that we were very disappointed with this technique.

In the rapid sequence group of Mirakhur *et al.* intubation was at 80–90 seconds after vecuronium and the onset of relaxation was 166 (SD 29.7) seconds. They comment that 'intubating conditions were clinically acceptable in all patients'. In our pancuronium 0.15 mg/kg group, maximum twitch depression was at 196.2 seconds, whilst in half the patients the intubating conditions were associated with coughing and bucking.

Abbott *et al.* gave vecuronium first, followed by thiopentone and then assessed the degree of relaxation 60 seconds after the loss of the eyelash reflex and at further 30-second intervals. They state that all patients were intubated after 60 seconds of loss of the eyelash reflex, and one patient had 3 minutes of apnoea. Thus the time between injection of vecuronium and intubation is not clear.

We agree that vecuronium is appropriate as part of a rapid sequence induction technique in penetrating eye

injury. However, we emphasise that intubation should not be attempted till at least 90 seconds after injection of the relaxant. Abbott mentions that intubation was only attempted if the anaesthetist considered a smooth intubation could be achieved. We suggest a nerve stimulator should be mandatory at this time to protect the injured eye.

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C. ORLIKOWSKI
C.G. STACK
R.J. ELTRINGHAM

A reply

We are not clear about the message in the letter by Drs Orlikowski, Stack and Eltringham. They have shown pancuronium, even in a dose of 0.15 mg/kg, to be an inappropriate choice for early intubation and thus unsuitable for a rapid sequence induction in situations where marked increases in intra-ocular pressure (IOP) are undesirable. We agree that it is an unsuitable agent because of a very prolonged block and undesirable cardiovascular effects associated with the use of such a big dose. We are in fact puzzled at their choice of pancuronium. There is no published evidence to show that pancuronium, in a dose of 0.15 mg/kg, acts more quickly than a similar dose of vecuronium (in fact their own experience shows the reverse) or that the intubating conditions are better with it when assessed at similar times after the relaxant administration. We however wholly support their conclusion that the use of vecuronium is appropriate as part of a rapid sequence induction technique in penetrating eye injuries, as was suggested by ourselves.

We have also shown that it is not only the particular agents used, but also the technique of induction that is important. The intubations in our rapid sequence induction group were not only carried out 80–90 seconds after vecuronium administration, but also at the peak effect of thiopentone. It might be interesting to know that the IOP changes can be further minimised by substituting propofol for thiopentone.¹ We are also surprised at the use of 0.2 mg/kg of vecuronium by Abbott and Samuel (*Anaesthesia*, 1987; 42: 1008–12) since not much is gained either in terms of improvement in intubating conditions or in the time to onset of action by increasing the dose of vecuronium

beyond 0.15 mg/kg^{2,3} Perhaps they might want to comment upon it themselves.

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R.K. MIRAKHUR

References

1. ELLIOTT P, MIRAKHUR RK, SHEPHERD WFI. Changes in intra-ocular pressure during rapid sequence induction of anaesthesia using propofol or thiopental with vecuronium. *Anesthesiology*, 1987; **67**: A483.
2. MIRAKHUR RK, FERRES CJ, CLARKE RSJ, BALI IM, DUNDEE JW. Clinical evaluation of Org NC45. *British Journal of Anaesthesia*, 1983; **55**: 119-24.
3. CASSON WR, JONES RM. Vecuronium induced neuromuscular blockade. The effect of increasing dose on speed of onset. *Anaesthesia*, 1986; **41**: 354-7.

A reply

The findings of Orlikowski *et al.* have amply demonstrated the inferior intubating conditions and onset times of pancuronium when compared with vecuronium. The lack of response to intubation in our patients may, as stated in our discussion, have been in part because of the presence of thiopentone rather than solely to neuromuscular blockade. A supplementary dose of 25-50 mg of thiopentone was given to all patients at 60 seconds after the loss of eyelash reflex in order to maintain anaesthesia. Vecuronium administration was immediately followed by the required dose of thiopentone. We used the loss of eyelash reflex as a starting point for timing because of individual variations in circulation time. We assume that within a few seconds of the thiopentone clinically acting on the brain, the vecuronium would have arrived at the musculature.

The purpose of our paper was to demonstrate whether a technique for rapid sequence anaesthesia with vecuronium can equate with suxamethonium in terms of dependable intubating conditions over a similar time period. This we have done. We entirely agree with nerve stimulator assessment of the degree of neuromuscular blockade before intubation is attempted, but it should be remembered that quite a few nonteaching hospitals are poorly endowed with such equipment. Thus we devised a method dependent on clinical observation and timing for use in such a situation.

Dr Sosis (*Anaesthesia* 1988; **43**: 247) has illustrated the different approach used in the United States in the anaes-

thetic management of penetrating eye injuries. The present authoritative teaching on this subject in Great Britain is to use non-depolarising muscle relaxants.¹ Suxamethonium raises intra-ocular pressure by increase in choroidal blood flow and by causing sustained contraction of extra-ocular muscles. This contraction produces a squeezing effect on the globe; an effect that has been well researched and confirmed.

The authors of the cited paper² were unable to find any evidence of a vitreous extrusion after the use of suxamethonium. However, they did not offer any evidence to show that the visual acuity in the damaged eyes had not deteriorated secondary to the globe-squeezing effect produced by suxamethonium. This squeezing effect produces intra-ocular pressure gradients that may cause further damage to the micro-anatomy of the retina and other intra-ocular structures. A small proportion of patients are going to present the anaesthetist with a higher risk of a failed intubation (severe facial injuries, stiff or ankylosed cervical vertebrae etc.) We agree with the use of suxamethonium in these cases, even at the expense of visual acuity. This is preferable to exposing the patient to the dangers of a long-acting non-depolarising muscle relaxant in the above mentioned situation.

The spectre of litigation that hangs over American doctors may have encouraged them to use suxamethonium. Some consider that pulmonary aspiration, though rare, could be relatively easy to prove when compared to proving the actual cause of an intra-operative deterioration in visual acuity. They therefore, play safe and use suxamethonium!

We hope that in Great Britain, anaesthetists resist such pressures and for this reason we continue to advocate the use of non-depolarising muscle relaxants in the rapid sequence induction of anaesthesia for the majority of these patients.

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M.A. ABBOTT

J.R. SAMUEL

References

1. ADAMS AK, JONES RM. Anaesthesia for eye surgery: general considerations. *British Journal of Anaesthesia* 1980; **52**: 663-9.
2. LIBONATI MM, LEAHY JJ, ELLISON N. The use of succinylcholine in open eye surgery. *Anesthesiology* 1985; **62**: 637-40.

Propofol and dystrophla myotonica

Dystrophla myotonica is a rare but serious inherited disorder which may pose substantial problems for the anaesthetist.¹ This is a report of the safe (and perhaps the first) use of propofol as an induction agent in a patient with this condition.

A 16-year-old boy was presented for manipulation of his foot for residual problems from his mild, but uncorrected, bilateral congenital talipes. The diagnosis of dystrophla myotonica was made when he was 7 years old. Pre-operative evaluation revealed a mentally retarded 50-kg youth with classical grip myotonia, bilateral ptosis and weakness of his facial musculature. There were no detectable cardiorespiratory problems and no previous anaesthetic history.

He was premedicated with temazepam 10 mg 2 hours before operation and he arrived in the anaesthetic room

calm, but not sedated. It was thought unlikely that he would tolerate either a gaseous induction or a regional anaesthetic technique. Thiopentone is probably contraindicated and Althesin which was suggested as suitable is no longer available. It was decided that propofol was perhaps the agent of choice. Anaesthesia was induced slowly over 90 seconds with propofol 80 mg and continued with the patient breathing spontaneously a mixture of nitrous oxide in oxygen supplemented with 0.5-2% isoflurane. Monitoring was instituted before induction and consisted of automated blood pressure, ECG and end-tidal CO₂ measurement. There was no evidence of respiratory or cardiovascular depression at induction or subsequently. His foot was successfully manipulated and plaster of Paris applied. The patient was unresponsive to painful stimuli at the conclusion of anaesthesia and for a further 20 minutes,

and then recovered rapidly in the usual manner after propofol anaesthesia.

He has since had a further two anaesthetics with the same agents with no problems apart from a prolonged waking time. On the third occasion a plantar fascia release was performed and a caudal injection of bupivacaine inserted under anaesthesia for postoperative pain relief. It is interesting to speculate on the cause of the prolonged recovery time. Anaesthesia lasted less than 10 minutes on the first two occasions and the concentration of isoflurane was maintained at 0.5% for application of the leg plaster. The induction dose of propofol was small and since it is known to have a rapid distribution half-life and metabolism, it appears unlikely to be the cause of the prolonged waiting time. These patients are known to demonstrate excessive somnolence possibly with a primary nervous system com-

ponent related to a decreased sensitivity to carbon dioxide.² However, there was no evidence of hypoventilation and carbon dioxide retention in this patient.

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K.A. MILLIGAN

References

1. KAUFMAN L. Anaesthesia in dystopia myotónica: a review of the hazards of anaesthesia. *Proceedings of the Royal Society of Medicine* 1960; 53: 183-8.
2. MILLER J, LEE C. Muscle diseases. In: KATZ J, BENUMOF J, KADIS LB, eds. *Anaesthesia and uncommon diseases: Pathophysiological and clinical correlations*. Philadelphia, PA: WB Saunders, 1981: 533-7.

Propofol infusions for status epilepticus

Recent publications about the effect of the anaesthetic induction agent propofol (Diprivan) on seizure threshold appear to be contradictory. The Committee on Safety of Medicines stated in August 1987, that it had 'received nine reports of convulsions and involuntary movements occurring in epileptics and nonepileptics during induction or emergence from anaesthesia induced by propofol'.¹ Simpson *et al.* compared propofol with methohexitone as the anaesthetic agents for electroconvulsive therapy (ECT) and found that seizure duration was markedly reduced after propofol.²

We support the study of Simpson *et al.* and report what we believe to be the first case of the use of propofol (Diprivan) for the control of status epilepticus. A 34-year-old Caucasian female with a known history of epilepsy and normally controlled on a regimen of phenytoin, chlormethiazole and diazepam, was admitted to the Accident and Emergency department after an overdose of chlormethiazole. She began to exhibit typical grand mal seizures after gastric lavage, which persisted sporadically for the next 5 days despite adequate serum levels of phenytoin and increasing doses of chlormethiazole. The fits became rapidly more frequent on the sixth day until they progressed to frank status epilepticus. Ventilation became increasingly compromised at the same time. This, together with a total inability to control her seizures, prompted the decision electively to ventilate her lungs mechanically. Tracheal intubation with an 8.0 mm cuffed Portex profile tube was performed on admission to the Intensive Therapy Unit, followed by propofol 120 mg and suxamethonium 100 mg. Controlled mechanical ventilation was instituted on a Servo 900c ventilator, using atracurium by infusion (rate of 30 mg/hour) to produce full muscle relaxation. All physical evidence of seizure activity was thereby abolished. We

consider that it is important to abolish the abnormal electrical activity of status epilepticus as well as its more obvious clinical effects. The patient was attached, by conventionally placed electrodes, to a cerebral function analysing monitor (CFAM) in order to monitor seizure activity. A propofol infusion was commenced at a rate of 6 mg/kg/hour, and further seizures were observed on the CFAM trace for the next 24 hours. Propofol was gradually withdrawn after this, and the patient rapidly regained consciousness. Extubation was carried out without further untoward effects, and the patient was discharged back to the ward the next day.

Propofol was chosen because work in this department has clearly demonstrated marked cortical depressant effect of the drug, with abolition of the visual evoked potential, at the infusion rate described above. We suggest that propofol may be extremely valuable in the intensive care treatment of status epilepticus, since unlike other commonly used drugs, the hangover effect following prolonged use is minimal.

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D. CHRISTMAS

References

1. Committee on Safety of Medicines. Current Problems No. 20, August 1987.
2. SIMPSON KH, HALSALL PJ, CARR CME, STEWART KG. Seizure duration after methohexitone and propofol for induction of anaesthesia for electro-convulsive therapy (ECT). *British Journal of Anaesthesia* 1987; 59: 1323P-4P.

Caudals and antisepsis—a response

In a comment (*Anaesthesia* 1988; 43: 158) on two photographs in our recently published book,¹ Dr Justins asks 'why do authors and anaesthetists treat the caudal approach to the epidural space so casually whilst they advocate more stringent rules for the lumbar approach to the same space?' He goes on to point out that one photograph 'shows a lumbar epidural needle inserted by a gloved and gowned anaesthetist' while another 'shows a caudal needle inserted by ungloved hands at the end of hairy arms'.

Authors and editors need broad shoulders (the hairy arms are an optional extra) to enable them to absorb criticism of their literary efforts and they usually remain silent, but the comment from Dr Justins requires a response. If he were to read our text, rather than simply look at the pictures, he would see that the points he makes are considered at some length (pp. 47 and 177). There is diversity of opinion among anaesthetists about the appropriate level of antiseptic technique required for various regional proce-

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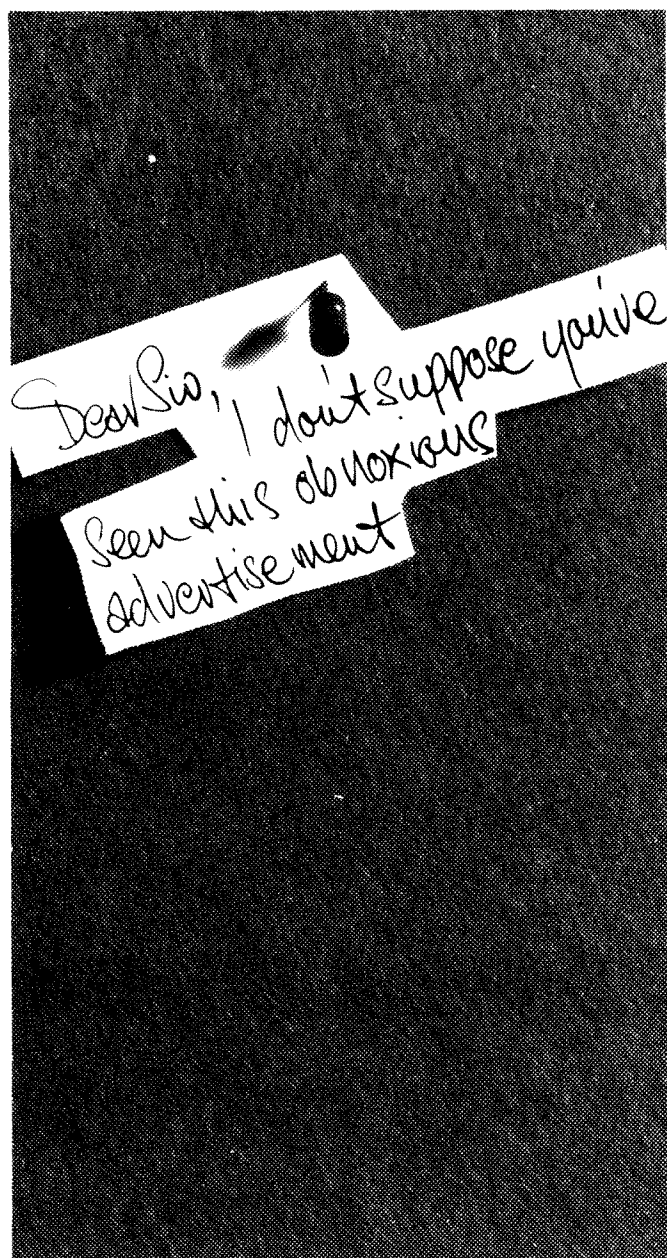
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dures. Our aim was that both our text and its illustrations should reflect that diversity.

However, Dr Justins' comments do highlight the genuine confusion which some anaesthetists feel when they are trying to establish a rational basis for their own practice. We suggest that it is more helpful to look at the question from the standpoint of pathology rather than anatomy; in other words, to consider what goes into the space, at what level and for how long, and the condition of the intervening tissues.

There are three reasons for taking stringent aseptic precautions when a lumbar epidural is performed. Firstly, in almost every case, an epidural catheter will be inserted and left in place for several hours or days. Like any other foreign body, the presence of a catheter may increase the risk of infection. Secondly, there is the possibility that the epidural needle or catheter may accidentally puncture the dura and enter the subarachnoid space. Cerebrospinal fluid is warm, contains sugar, has no blood supply and is an ideal culture medium. Thirdly, it is virtually impossible to insert a catheter without handling it. On the other hand, it is not customary to insert a catheter for a sacral epidural

and the procedure may be performed with a truly no-touch technique. It is evident that the risks of introducing infection are very different for the two methods. Routine gloving and gowning may induce a sense of false security, may encourage the anaesthetist to underestimate the importance of these basic pathological principles and will not necessarily prevent infection and abscess formation. The one case of epidural abscess known to us occurred after an obstetric epidural performed at 0300 hours by a sleepy (but fully gloved and gowned) resident.

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Brighton*

J.A.W. WILDSMITH

E.N. ARMITAGE

Reference

1. WILDSMITH JAW, ARMITAGE EN. Principles and practice of regional anaesthesia. Edinburgh: Churchill Livingstone, 1987.

Difficult extubation

Lal¹ advocated a hook method in a case of difficult extubation; we have experience of this problem and used a method which is more practical than the hook method.

A healthy 35-year-old primigravida, of average build, required emergency lower segment Caesarean section. Her premedication consisted of atropine, 0.6 mg intramuscularly 30 minutes before induction and metoclopramide, 10 mg intravenously during pre-oxygenation. Anaesthesia was induced with sodium thiopentone 350 mg. Tracheal intubation was easily performed with a 8-mm Rusch cuffed tube after muscle paralysis with suxamethonium 75 mg. Anaesthesia was maintained with N₂O, O₂, halothane 0.5%, pancuronium, and ventilation of the lungs was controlled. The operation lasted 65 minutes and was uneventful. The muscle relaxant was reversed with neo-

stigmine 2.5 mg and atropine 1.2 mg, and extubation was attempted but failed. The tube could be rotated in its place, but it could not be pulled out using even substantial force or even after relaxation with suxamethonium 25 mg. It was possible that a fold had formed at the distal end of the cuff since the tracheal tube was old. It had been in use for over a year and had been repeatedly boiled. Smoothing the fold with 1 ml air or catching the portion of the cuff above the rim of glottidis with a skin hook also proved futile. This caused linear tears in the cuff but did not unfold it. We used long, curved, Bozemann uterine dressing forceps to catch the cuff, after one blade was introduced through the rent made in it (Fig. 1). The fold of the cuff could thus be pulled out and the patient's trachea extubated. The blades of these forceps have serrations and provide greater surface area for bearing the force of extraction.

She developed severe sore throat after the operation and, on the third day a small greyish laryngotracheal membrane could be seen on indirect laryngoscopy. The patient refused to have this excised. She spoke with a slightly gruff voice but the sore throat resolved at discharge.

The chance of damage is minimal with this method and we think it is preferable.

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Aligarh Muslim University,
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R.M. KHAN
T.Z. KHAN
M. ALI
M.S.A. KHAN

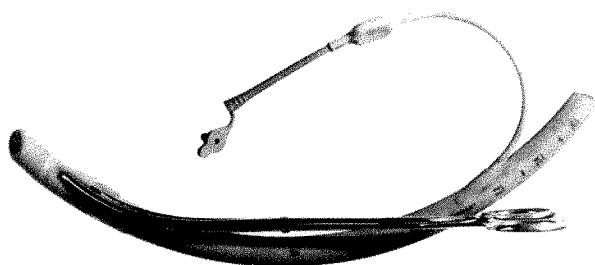


Fig. 1.

Reference

1. LAL NG. Difficult extubation. *Anaesthesia* 1980; **35**: 500-1.

Allen's test performed by pulse oximeter

Allen's test is one of the routine pre-anaesthetic tests for patients who require cannulation of the radial artery in order to monitor continuous blood pressure and for blood gas samples.¹

Cooperation by the patients is required but sometimes we are confronted with uncooperative or unconscious patients, or ones with whom we cannot communicate because of language difficulties, or young children, or the

patient with multiple injuries, when the Allen test cannot be performed satisfactorily.

We use a pulse oximeter (Nellcor) in these patients to confirm a good blood supply to both ulnar and radial arteries.² We connect the probe to one of the fingers and occlude by digital pressure both arteries until the pulse oximeter shows no pulsations on the screen. We then release the pressure on radial artery and check the display for pulsations. We again occlude the artery until occlusion is complete and release the pressure from the ulnar artery. When there is blood flow through the ulnar artery, pulsations appear again on the screen.

These findings confirm a good collateral supply and cannulation of radial artery can be performed in safety.

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B. ROZENBERG
M. ROSENBERG
J. BIRKHAN

References

1. MULLER RD. *Anesthesia*, Vol. 1. New York: Churchill-Livingstone, 1986: 435.
2. YELDERMAN M. New Evaluation of pulse oxymetry. *Anesthesiology* 1983; 59: 349-52.

Unstable cervical fracture

Dr Braude's letter (*Anaesthesia* 1987; 42: 1334) which commented on the case described by Eason and colleagues¹ of general anaesthesia for emergency Caesarean section in a woman with an unstable cervical fracture, gives the impression that awake fiberoptic intubation would have been the method of choice for this patient, and that this would be a view widely held in the United States of America.

Dr Eason pointed out that awake intubation, even by an experienced operator, can cause quite violent coughing with movement of the head and neck and which could negate the theoretical advantage of the technique. This has led at least one group in the USA² to question the thesis that patients' interests are always best served by an awake procedure. In addition, for an awake fiberoptic procedure to be safely undertaken the patient must be cooperative, which Dr Eason's patient could not be relied upon to be. Dr Eason's problems were compounded by the fact that his patient was at risk from regurgitation. Is a patient with a topically anaesthetised glottis at any less risk of aspiration than a patient whose laryngeal reflexes are obtunded by general anaesthesia?

Our own experience has changed our practice when anaesthetising patients with unstable cervical spines.

We have found the procedure of fiberoptic tracheal intubation under topical anaesthesia alone to be poorly

tolerated by patients, and energetic coughing is often a feature. If sedation is added³ (midazolam) we have found it all too easy to cross the thin dividing line between sedation and anaesthesia. We have thus abandoned awake procedures and now use the fiberoptic laryngoscope whilst the patient is breathing halothane in oxygen through a nasal airway.

We would not claim that this (or any other) method would have been the best in the case described by Eason *et al.* It is merely what we would have done if faced as they were by the kind of situation in which 'gentlemen now abed in England' would think themselves jolly lucky they were not there.

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A.J.ORDMAN
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References

1. EASON JR, SWAINE CN, JONES PIE, GRONOW MJ, BEAUMONT A. Unstable cervical fracture. Anaesthetic management for an urgent caesarean section. *Anaesthesia* 1987; 42: 745-9.
2. WELLS DG, TREDERA CR. Intubation of the patient with cervical spine injury. *Anaesthesia and Intensive Care* 1987; 15: 353-4.
3. WHITLOCK JE, CALDER I. Transillumination in fiberoptic intubation. *Anaesthesia* 1987; 42: 570.

Cardiovascular collapse after epidural anaesthesia for Caesarean section

It was predictable that much of the correspondence (*Anaesthesia* 1987; 42: 1226-30) regarding Dr Alderson's case report (*Anaesthesia* 1987; 47: 643-5) would centre around inadequate invasive monitoring, the use of a large bolus dose of local anaesthetic into the epidural space and the defence of regional anaesthesia in a complicated obstetric patient. The use of general anaesthesia and its comparative advantages in this case have been disregarded.

The incidence of hypotension associated with epidural anaesthesia for Caesarean section is more than 80% without the use of preventive measures¹ such as fluid loading, the administration of ephedrine (both relatively contraindicated in this case) and displacement of the uterus to the left. Even with these measures and the administration of incremental doses of local anaesthetic, transitory hypotension occurs in 16% of patients with otherwise normal cardiovascular systems.² Extensive sympathetic blockade is an unavoidable accompaniment of regional anaesthesia for Caesarean section.³ This patient's reliance on cardiac

sympathetic drive had already been demonstrated by the development of pulmonary oedema in response to administration of labetalol, so epidural anaesthesia does not appear to be inherently the most stable choice from a cardiovascular point of view.

General anaesthesia, besides the specific problems associated with pregnancy, carries the danger of myocardial depression by both induction and inhalational agents. These effects, however, are compensated for by vasodilation, decreased venous return associated with controlled ventilation of the lungs and an intact sympathetic system to respond to these changes. Cardiac failure only occurs in 3-9% of patients with aortic regurgitation during pregnancy,⁴ but its presence is an ominous sign. General anaesthesia is probably a safer alternative under such conditions, because there is less potential for catastrophic alterations in coronary perfusion pressure and heart rate, and any adverse changes are likely to be easier to treat in a situation in which adequate oxygenation and ventilation

are more assured. My comments do not include patients with cardiac disease who require either epidural analgesia for vaginal delivery, or those without cardiac failure who require Caesarean section.

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References

1. SHNIDER SM, LEVINSON G. Anesthesia for Caesarian Section. In: SHNIDER SM, LEVINSON G, eds. *Anaesthesia for obstetrics*, 2nd edn. Baltimore: Williams and Wilkins, 1987: 254-75.
2. THORBURN J, MOIR DD. Epidural analgesia for elective Caesarean section. Technique and its assessment. *Anaesthesia* 1980; **35**: 3-6.
3. CRAWFORD JS. Principles and practice of obstetric anaesthesia, 5th edn. Oxford: Blackwell, 1984.
4. MANGANO DT. Anaesthesia for the pregnant cardiac patient. In: SHNIDER SM, LEVINSON G, eds. *Anaesthesia for obstetrics*, 2nd edn. Baltimore: Williams and Wilkins, 1987: 343-81.

A reply

I agree with these comments. There is in my opinion a group of cardiac conditions in which the patient's cardiac

function may be considerably compromised by the sympathetic blockade produced by epidural or spinal anaesthesia for Caesarean section. This group includes aortic stenosis,¹ severe coronary disease,¹ Eisenmenger's syndrome and pulmonary hypertension² and hypertrophic obstructive cardiomyopathy.³ To this list I add severe aortic incompetence as a result of my experience.

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References

1. BONICA J, UELAND K. Heart disease. In: BONICA J, ed. *Principles and practice of obstetric analgesia and anaesthesia*. Philadelphia: F. A. Davis, 1972: 941-77.
2. JOYCE TH. Cardiac disease. In: JAMES FM III, WHEELER AS, eds. *Obstetric anaesthesia: the complicated patient*. Philadelphia: F. A. Davis, 1982: 87-101.
3. OAKLEY GDG, MCGARRY K, LIMB DG, OAKLEY CM. Management of pregnancy in patients with hypertrophic cardiomyopathy. *British Medical Journal* 1979; **1**: 1749-50.

An unusual ventilator valve failure

We are certain that most anaesthetists who use Siemens Servo 900 series ventilators will be aware of the Hazard Warning¹ which relates to the failure of the silicone rubber expiratory valves used in these machines.

We experienced several valve failures during 1987 which were rapidly detected by the ventilator's monitoring system. These valves all had a circumferential split through the full thickness of the silicone rubber.

We report the mode of failure of one of these valves, which appeared to be different from previous failures. This

particular valve appeared to be intact when it was removed from the ventilator (Fig. 1). However when the valve was stretched slightly (Fig. 2) a circumferential depression could be seen. This depression was over a split in the inner surface of the valve, which had not involved the full thickness of the silicone rubber.

Discussions with the manufacturers suggest that this is an unusual mode of valve failure and that the valve was made with a formulation of silicone rubber no longer in production.

Its failure leads us to suggest that expiratory valves in these machines should be removed for careful inspection in the case of an otherwise unexplained ventilator failure.

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D.W. BETHUNE
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Reference

1. DHSS. HN (Hazard) (87) 1.

A reply

Siemens-Elma have received reports of premature failure of the silicone rubber expiratory valve. Investigations continue into the possible causes for this 'peculiar' phenomenon, peculiar, in the context of an event which occurs at some hospitals, whilst the majority of other hospitals do not experience failure.

The particular observation described by Dr Kneeshaw is interesting because it suggests that the origin of the fracture is on the inside surface of the valve. The particular silicone formula involved with this valve has been discontinued but this report of a possible fracture from the inside will be useful for future analyses.

We agree with the suggestion that the valve could be inspected; we also urge caution because the valve should not be stretched.

Siemens Ltd,
Sunbury on Thames,
Middlesex TW16 7HS

R. HOWELL

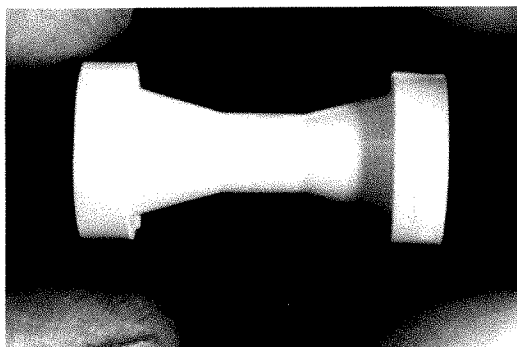


Fig. 1. Silicone rubber expiratory valve as removed from the ventilator.

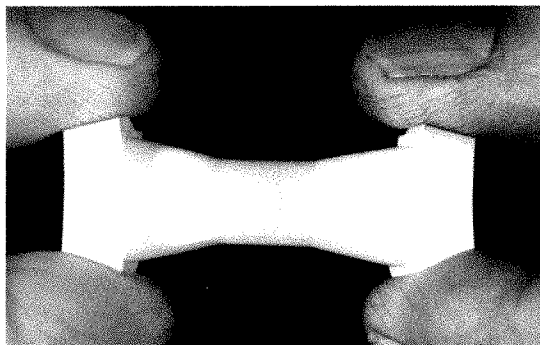


Fig. 2. Stretching the valve slightly shows the split, which has formed inside the valve and is not yet through to the outer circumference.

Another advantage of the paramedian approach?

Dr Meiklejohn, in his *in vitro* study of the effect of rotation of an epidural needle with the epidural space (*Anaesthesia* 1987; 42: 1180-2), found that this manoeuvre increased significantly the risk of dural puncture. He recommended that the bevel of the needle be inserted perpendicular to the fibres of the interspinous ligament and ligamentum flavum in order to avoid this complication. It is my practice and probably that of many other anaesthetists, when the midline approach is used, to split the fibres of these ligaments and so to reduce the trauma involved by passage of a 16-G needle. The nonrotational technique, therefore, may increase the incidence and severity of backache after an epidural, though this remains to be proven. Furthermore, for anaesthetists accustomed to using a winged Tuohy needle, the practical difficulties of insertion of the bevel perpendicular to the fibres of the ligaments, needs to be considered.

A solution to this problem would be to use the paramedian approach to the epidural space to which there are

many claimed advantages over the midline route;^{1,2} the bevel enters the epidural space at an oblique angle, the risk of dural puncture may be reduced and passage of the catheter facilitated. Furthermore, the technique needs no re-direction of the bevel of the Tuohy needle within the epidural space, which may be particularly significant in the light of Dr Meiklejohn's findings.

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References

1. CARRIE LES. The paramedian approach to the epidural space. Technique and choice of needle. *Anaesthesia* 1977; 32: 670-1.
2. ARMITAGE EN. The paramedian approach to lumbar epidural analgesia. *Anaesthesia* 1976; 31: 1287-8.

A problem with the Medex fast-flush device

A Medex fast-flush device attached to an arterial line has become jammed in the open position on four occasions in a one-year period. This resulted in the rapid infusion of a 500-ml bag of heparinised saline. This has occurred at the hands of four different ITU trained nurses, so I believe this potential problem should be emphasized.

This device includes a fixed resistance for continuous slow flush, a transducer diaphragm, and a fast-flush control. The latter is operated by a pinch manoeuvre of a plastic casing, which pulls a rubber flap that, in turn, opens the lumen of the device. There are two plastic hinges above the rubber flap designed to prevent removal of the plastic

casing. Over-zealous tugging at the plastic casing can cause it to lock over one of the hinges, which puts the system permanently in the fast-flush mode.

No harm came to any patient but obviously there are patients who will poorly tolerate such a sudden fluid load. It is recommended that this problem be drawn to the attention of ITU staff and the manufacturers intend to re-iterate their advice about careful handling in the future.

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M.R. DRESNER

Isoflurane in a drawover anaesthetic system

The letter by Yoganathan and Houghton (*Anaesthesia* 1987; 42: 1241) was of interest, but would have been much more so if supported by data. It seems inappropriate to compare isoflurane with halothane alone since Houghton himself advocated the additional use of trichloroethylene, considering that 'halothane is not an outstanding anaesthetic when used as a sole inhalational agent'.¹ Hollis was of a firmer opinion.² Such work also duplicates many well documented comparisons.³ We have recently demonstrated that isoflurane alone is an acceptable alternative to the halothane-trichloroethylene combination.⁴ One could therefore reasonably expect that it would be even more acceptable when compared to halothane alone.

Yoganathan and Houghton were apparently using a face mask; we considered it better to intubate, since military casualties are at great risk of aspiration. We then ventilated our patients' lungs for a short period, finding the two groups to be similarly simple, safe and uncomplicated during induction and maintenance for any duration of surgery, unlike the latter authors. It is my experience that surgical anaesthesia is very difficult to achieve using the Triservice anaesthetic apparatus (TSA) without this period of manual ventilation of the lungs regardless of the volatile agent used. We recommended this technique to ensure that inexperienced personnel would be able to use the apparatus

successfully. Despite the authors' obvious experience it is surprising that they did not have difficulty with halothane induction let alone isoflurane.

Yoganathan and Houghton state that isoflurane causes more respiratory depression than halothane, but the reference they quote examined unstimulated volunteers.⁵ They contradict several publications which show little difference between halothane and isoflurane in this respect during surgical stimulation, which is the more clinically relevant situation.³ We confirmed a lower respiratory rate at the same $PECO_2$ with isoflurane, which is preferable.

It is now my preference to use muscle relaxants (vecuronium) and controlled ventilation in all patients when the TSA is used and not just when using isoflurane. The respiratory depression, oxygen waste and prolonged recovery associated with spontaneous ventilation of any inhalational agent is unacceptable in the field. The ratio of the maximum output of isoflurane from the TSA to its minimum anaesthetic alveolar concentration is quite sufficient clinically, in my experience. The vaporizer might need to be warmed in very cold environments.

Isoflurane administration is expensive, but in the military environment this is surely inconsequential when compared to the overall cost of operating a field hospital and the cost of the weapons making anaesthesia necessary. Isoflurane

has many advantages for military use with the TSA and I still consider it to be the ideal agent when one is confident of its effects in hypovolaemia.

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S.Q.M. TIGHE

References

1. HOUGHTON IT. The Triservice anaesthetic apparatus. *Anaesthesia* 1981; 36: 1094-108.
2. HOLLIS N. Halothane and trichloroethylene. Two agents in a single vaporizer. *Anaesthesia* 1986; 41: 309-15.
3. EGER E I II. *Isoflurane (Aerrane). A compendium and reference*. 2nd edn. BOC Inc., 1985.
4. TIGHE SQM, PETHYBRIDGE RJ. A comparison of halothane and trichloroethylene with isoflurane. A study of drawover anaesthesia with the Triservice anaesthetic apparatus. *Anaesthesia* 1987; 42: 887-91.
5. FOURCADE HE, STEVENS WC, LARSON CP, CROMWELL TH, BAHLMAN SH, HICKLEY RF, HALSEY MJ, EGER E I II. The ventilatory effects of Forane, a new inhaled anesthetic. *Anesthesiology* 1971; 35: 26-31.

Epidural morphine and headache secondary to dural puncture

Various modes of treatment have been employed for the prophylaxis and treatment of the postdural puncture headache. We studied the use of epidural morphine in 15 patients (40-70 years old) who were to have major urological procedures but who had inadvertent dural puncture during placement of lumbar epidural catheters.

Epidural catheters were inserted through a 17-gauge Tuohy needle for the management of postoperative pain. The epidural catheter was successfully placed on a repeat attempt after dural puncture. All patients were admitted routinely to the intensive care unit for postoperative management; 5 mg morphine sulphate in 10 ml was introduced into the epidural space. Subsequent 5 mg doses were administered as needed. Total dose averaged 20 (SD 4.8) mg over 41.7 (SD 18.5) hours. All patients assumed the upright position within 24 hours and were followed for the development of headache over 5 postoperative days. None of the patients developed post dural puncture headache.

This work suggests that epidural morphine is an effective prophylaxis for post dural puncture headache. The results are significant in the light of Crawford's findings that 70%

of a series of 269 obstetric patients with inadvertent dural puncture developed this complication.¹ It should be noted that administration of epidural morphine is occasionally associated with respiratory depression. Thus, it should only be used in situations where the patient can be closely monitored.

It is our impression that in patients who suffer inadvertent dural puncture, and in whom an epidural catheter can be properly placed on repeat attempt, epidural morphine is effective as prophylaxis for post dural puncture headache.

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Reference

1. CRAWFORD JS. Headache after lumbar puncture. *Lancet* 1981; 2: 418.

Replacement of tracheostomy tubes

The process of change of a tracheostomy tube soon after operation can be hazardous, if this has to be done before a definitive, epithelialised, fistula has developed. We have successfully employed a simple method which uses a modification of the ubiquitous 'railroad' technique. Instead of a solid bougie however, a well lubricated, plain, uncut, oral or nasal PVC tracheal tube is used as a guide tube. The tube should be of a diameter just smaller than the internal diameter of the tracheostomy tube.

The guide is well lubricated, the connector only lightly applied and with the breathing system connected, 8 or 10 centimetres of the guide tube is passed into the lumen of

the tracheostomy tube. The connector can now easily be removed to allow withdrawal of the old tracheostomy tube and its replacement with a new one; the whole procedure is completed by the removal of the guide tube.

The airway is secure at all times, so the changeover can be gentle and unhurried and ventilation (if required), need only be interrupted during the few seconds that the connector is removed.

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J. RICHARDSON
P. BICKFORD SMITH

A modification of the Ohmeda vaporizer filler

Most members of the Anaesthetic Department at this hospital have experienced some difficulty with filling the Ohmeda Tech IV vaporizers. A 6-inch plastic filler is supplied but it is difficult to remove the airlocks from the system, which makes filling at times impossible, and there has been considerable leakage with wastage of anaesthetic agent. Apart from pollution, this is particularly important when isoflurane is used because of the high cost of the agent. An additional problem is that some of the fillers have fractured at the upper end as they are stiff and non-pliable.

We were supplied with modified 'ball-valve' fillers after complaints to the manufacturer. These improved the

situation to some extent but there were still occasions when we were unable to fill the vaporizers. Our biomedical service has modified some of the fillers to our specifications. These are now more effective: 12 inches long with flexible plastic tubing. They are easier to use, have few airlocks and there is no waste. We suggest other anaesthetists who experience this problem should follow our example.

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K.R. EDGE

A reply

It is possible that the correct filling instructions are not being followed by Dr Edge and his colleagues. Our experience shows that airlocks can occur if the pressures within the vaporizer and bottle are not equalized. If our latest filling instructions are used in conjunction with the latest bottle adaptors, and there are still problems, further investigation is needed to establish the cause.

We were unable in the development of our current bottle adaptor to find a tube material which was more flexible than the existing one but which did not deteriorate at a much faster rate. A typical example is a flexible PVC

tubing which releases plasticiser at a dramatic rate when placed in contact with liquid drug or saturated vapour. If Dr Edge has identified a more suitable material then it may be of value to us and we would welcome details.

Provided that the new bottle adaptors are used in accordance with our instructions, then we remain firm in our belief that they provide a solution which has proved to be generally acceptable in terms of quality, reliability and overall user convenience.

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West Yorkshire BD20 6RB*

A.J.W. WALL

Anaesthetic literature

This section of *Anaesthetic literature* contains references taken from *Current Contents—Life Sciences* for February 1988. The Journals which may be consulted when *Anaesthetic literature* is compiled are those listed in *Current Contents—Life Sciences*, published by the Institute of Scientific Information, Philadelphia, Pennsylvania, USA.

Pharmacology

Adrenergic drugs and their antagonists

- A low molecular weight brain substance interacts, similarly to clonidine, with alpha 2-adrenoceptors of human platelets. DIAMANT S, ELDOR A, ATLAS D. *European Journal of Pharmacology* 1987; 144: 247.
- Intravenous clonidine produces hypoxemia by a peripheral alpha-2 adrenergic mechanism. EISENACH JC. *Journal of Pharmacology and Experimental Therapeutics* 1988; 244: 247.
- Beta-adrenergic blockers. FRISHMAN WH. *Medical Clinics of North America* 1988; 72: 37.
- Alpha-adrenergic blocker for posthernioplasty urinary retention: Prevention and treatment. GOLDMAN G, LEVIAT A *et al. Archives of Surgery* 1988; 123: 35.
- Tulobuterol: a full beta-adrenoceptor agonist or a partial beta-agonist with membrane stabilizing activity? GONZALES-SICILLIA L, PEREZ-OJEDA E *et al. General Pharmacology* 1988; 19: 103.
- High capacity for pulmonary first-pass elimination or propranolol in rats. IWAMOTO K, WATANABE J, AOYAMA Y. *Journal of Pharmacy and Pharmacology* 1987; 39: 1049.
- The pulmonary vascular effects of dopamine, dobutamine, and isoproterenol in unilobar pulmonary edema in dogs. LIGHT RB, ALI J *et al. Journal of Surgical Research* 1988; 44: 26.
- Role of beta 1-adrenoceptors in hypertensive cardiac hypertrophy. LINDPAINTNER K, SEN S. *Journal of Hypertension* 1987; 5: 663.
- Calcium entry blocking drugs—their classification and sites of action in smooth muscle cells. RAEBURN D. *Medical Biology* 1987; 65: 175.
- The pharmacology of dobutamine. RUFFOLO RR. *American Journal of the Medical Sciences* 1987; 294: 244.
- Stereoselective delivery and actions of beta receptor antagonists. WALLE T, WEBB JG *et al. Biochemical Pharmacology* 1988; 37: 115.

Anaesthetic agents

- A single injection of diazepam induces long-lasting sensitization. ANTELMAN SM, KOCAN D *et al. Psychopharmacology Bulletin* 1987; 23: 430.
- A comparison of the central and peripheral antimuscarinic effects of atropine and methylatropine injected systemically and into the cerebral ventricles. BREZENOFF HE, XIAO YF, VARGAS H. *Life Sciences* 1988; 42: 905.
- Ketamine effects on local cerebral blood flow and metabolism in the rat. CAVAZZUTI M, PORRO CA *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; 7: 806.
- Haemodynamic changes during anaesthesia induced and maintained with propofol. CLAEYS MA, GEPTS E, CAMU F. *British Journal of Anaesthesia* 1988; 60: 3.
- Opioid mechanisms of some behavioral effects of ketamine. FIDECKA S. *Polish Journal of Pharmacology and Pharmacy* 1987; 39: 353.
- Some ventilatory effects of propofol as sole anaesthetic agent. GOODMAN NW, BLACK AMS, CARTER JA. *British Journal of Anaesthesia* 1987; 59: 1497.

- Nitrous oxide anesthesia in patients with ischemic chest discomfort—effect on beta-endorphins. O'LEARY U, PUGLIA C *et al. Journal of Clinical Pharmacology* 1987; 27: 957.
- Minireview: Adrenocortical suppression and other endocrine effects of etomidate. PREZIOSI P, VACCA M. *Life Sciences* 1988; 42: 477.
- Toluene, halothane, 1,1,1-trichloroethane and oxazepam produce ethanol-like discriminative stimulus effects in mice. REES DC, KNISELY JS *et al. Journal of Pharmacology and Experimental Therapeutics* 1987; 243: 931.
- GABA involvement in naloxone induced reversal of respiratory paralysis produced by thiopental. SURIA A, NASREEN R, SAEED SA. *Life Sciences* 1988; 42: 643.
- Changes in intraocular pressure associated with administration of propofol. VANACKER B, DEKEGEL D *et al. British Journal of Anaesthesia* 1987; 59: 1514.
- Ketamine-induced and morphine-induced analgesia and catalepsy. 1. Tolerance, cross-tolerance, potentiation, residual morphine levels and naloxo action in rat. WINTERS WD, HANCE AJ *et al. Journal of Pharmacology and Experimental Therapeutics* 1988; 244: 51.
- Effect of halothane on sinus rhythm of dog heart in situ. YOSHIDA T, NAKAJIMA T. *Archives internationales de Pharmacodynamie et de Therapie* 1987; 290: 36.

Analgesic agents

- Effects of codeine, morphine and a novel opioid pentapeptide BW443C, on cough, nociception and ventilation in the un-anaesthetized guinea-pig. ADCOCK JJ, SCHNEIDER C, SMITH TW. *British Journal of Pharmacology* 1988; 93: 93.
- Naloxone excites oxytocin neurones in the supraoptic nucleus of lactating rats after chronic morphine treatment. BICKNELL RJ, LENG G *et al. Journal of Physiology* 1988; 396: 297.
- Intraoperative administration of buprenorphine vs methadone in postoperative pain management. CARTA F, CERVI D *et al. Current Therapeutic Research* 1987; 42: 1003.
- Nalbuphine—an autoradiographic opioid receptor binding profile in the central nervous system of an agonist antagonist analgesic. DESOZA EB, SCHMIDT WK, KUJAR MJ. *Journal of Pharmacology and Experimental Therapeutics* 1988; 244: 391.
- Antinociceptive effects of the novel opioid peptide BW443C compared with classical opiates; peripheral versus central actions. FOLLENFANT RL, HARDY GW *et al. British Journal of Pharmacology* 1988; 93: 85.
- Delayed muscular rigidity and respiratory depression following fentanyl anesthesia. KLAUSNER JM, CASPI J. *Archives of Surgery* 1988; 123: 66.
- Buprenorphine detoxification from opioid dependence: a pilot study. KOSTEN TR, KLEBER HD. *Life Sciences* 1988; 42: 635.
- Pharmacokinetics of different epidural sites of morphine administration. NORDBERG G, HANSDOTTIR V *et al. European Journal of Clinical Pharmacology* 1987; 33: 499.
- Influence of adrenergic and cholinergic mechanisms in baclofen induced analgesia. TAMAYO L, RIPO J, CONTRERAS E. *General Pharmacology* 1988; 19: 87.

The collator of this section is Dr L. Kaufman, MD, FFARCS, Anaesthetic Office, The Rayne Institute, University College, University Street, London WC1E 6JJ. Dr Kaufman is prepared to provide on request a new additional service to our readers. References from January 1984 have been entered on a data base using Dbase III Plus (MsDos) and this will be upgraded in the near future to Dbase IV. The program which provides search facilities will be available free of charge save for the cost of the disk. In addition, all the data on a yearly or monthly basis will be available at a modest charge. Enquiries direct to Dr Kaufman at the above address please.

Morphine-like discriminative stimulus effects of opioid peptides; possible modulatory role of D-Ala²-D-Leu⁵-enkephalin (DADL) and dynorphin A(1-13). UKAI M, HOLTZMAN SG. *Psychopharmacology* 1988; **94**: 32.

Muscle relaxants

Morphologic changes in the muscles of patients with postpolio-myelitis neuromuscular symptoms. DALAKAS MC. *Neurology* 1988; **38**: 99.

Vecuronium induced bradycardia following induction of anaesthesia with etomidate or thiopentone, with or without fentanyl. INOUE K, ELBANAYOSY A *et al.* *British Journal of Anaesthesia* 1988; **60**: 10.

Genetic factors in myasthenia gravis—a family study. KERZINSTORR L, METCALFE RA *et al.* *Neurology* 1988; **38**: 38.

Other drugs

Is the intrinsic sympathomimetic activity of pindolol beta 2-adrenoceptor selective? AELLIG WH, CLARK BJ. *British Journal of Clinical Pharmacology* 1987; **24** (Suppl. 1): 21S.

Intranasal drug delivery for systemic medications. CHIEN YW, CHANG SF. *CRC Critical Reviews in Therapeutic Drug Carrier Systems* 1987; **4**: 67.

Compartmental model analysis in pharmacokinetics. FLEISHAKER JC, SMITH RB. *Journal of Clinical Pharmacology* 1987; **27**: 922.

Hepatic vs gastrointestinal presystemic extraction of oral midazolam and flurazepam. GREENBLATT DJ, EICHELKRAUT W *et al.* *Journal of Pharmacology and Experimental Therapeutics* 1987; **243**: 852.

The influence of drugs on nasal ciliary movement. HERMANS WAJJ, MERKUS FWHM. *Pharmaceutical Research* 1987; **4**: 445.

Warfarin: metabolism and mode of action. PARJ BK. *Biochemical Pharmacology* 1988; **37**: 19.

Recent advances in drug delivery technology for neurology. STAHL SM, WETS KM. *Clinical Neuropharmacology* 1988; **11**: 1.

Apparatus

Epidural administration of opiates by a new device. AHLGREN FIH, AHLGREN MBE. *Pain* 1987; **31**: 353.

The possibility of using narrow tubes in anesthesia. BRONSTEIN G, GESZTES TH, PUTERMAN M. *Current Therapeutic Research* 1987; **42**: 1033.

The use of intermittent and continuous recordings of jugular venous bulb oxygen saturation in the unconscious patient. GARLICK R, BIHARI D. *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47** (Suppl. 188): 47.

Inaccurate oxygen delivery in some portable liquid oxygen devices. MASSEY LW, HUSSEY JD, ALBERT RK. *American Review of Respiratory Disease* 1988; **137**: 204.

Complications

Cardiac arrest associated with coronary artery spasm. FELLOWS CL, WEAVER WD, GREENE HL. *American Journal of Cardiology* 1987; **60**: 1397.

Metoprolol-induced hepatitis: rechallenge and drug oxidation phenotyping. LARREY D, HENRION J *et al.* *Annals of Internal Medicine* 1988; **108**: 67.

Can postoperative pulmonary complications after elective cholecystectomy be predicted. POE RH, KALLAY MC *et al.* *American Journal of the Medical Sciences* 1988; **295**: 29.

A nurse-associated epidemic of cardiac arrests in an intensive care unit. SACKS JJ, STROUP DF *et al.* *Journal of the American Medical Association* 1988; **259**: 689.

Unexpected vascular response to epinephrine in port wine stains. SMOLLER BR, KWAN TH, NOE JM. *Plastic and Reconstructive Surgery* 1987; **80**: 784.

Risk factors for intubation injury of the larynx. VOLPI D, LIN PT *et al.* *Annals of Otolaryngology, Rhinology and Laryngology* 1987; **96**: 684.

General anaesthetic procedures

Priming with nondepolarizing relaxants for rapid tracheal intubation: a double-blind evaluation. BAUMGARTEN RK, CARTER CE *et al.* *Canadian Journal of Anaesthesia* 1988; **35**: 5.

A comparative study of conventional versus high-frequency jet ventilation with relation to the incidence of postoperative morbidity in thoracic surgery. NEVIN M, VAN BESOUW JP *et al.* *Annals of Thoracic Surgery* 1987; **44**: 625.

Painless lithotripsy: experience with 100 patients. PHILP T, KELLETT MJ *et al.* *Lancet* 1988; **1**: 41.

Major abdominal operations on patients aged 80 and over: an audit. POLLOCK AV, EVANS M. *British Medical Journal* 1987; **295**: 1522.

The prevention of pulmonary complications after upper abdominal surgery in patients with noncompromised pulmonary status. ROUKEMA JA, CAROL EJ, PRINS JG. *Archives of Surgery* 1988; **123**: 30.

General interest

What is included in clinical competence? COX K. *Medical Journal of Australia* 1988; **148**: 25.

Clinical pharmacological and therapeutic considerations in general intensive care: a review. FARINA ML, BONATI M *et al.* *Drugs* 1987; **34**: 662.

A case of ACTH-producing pheochromocytoma. SAKURAI H, YOSHIIKE Y *et al.* *American Journal of the Medical Sciences* 1987; **294**: 258.

Local analgesia

Pharmacokinetics of lidocaine and bupivacaine and stable isotope labelled analogues: a study in healthy volunteers. BURM AGL, DE BOER AG *et al.* *Biopharmaceutics and Drug Disposition* 1988; **9**: 85.

Does diazepam really reduce the cardiotoxic effects of intravenous bupivacaine? GREGG RV, TURNER PA *et al.* *Anesthesia and Analgesia* 1988; **67**: 9.

Cardiac electrophysiologic effects of lidocaine and bupivacaine. MOLLER RA, COVINO BG. *Anesthesia and Analgesia* 1988; **67**: 107.

Spinal and epidural analgesia

Unexpected cardiac arrest during spinal anesthesia: a closed claims analysis of predisposing factors. CAPLAN RA, WARD RJ *et al.* *Anesthesiology* 1988; **68**: 5.

Spinal opioids

Intrathecal sufentanil as a supplement to subarachnoid anaesthesia with lignocaine. DONADONI R, VERMEULEN H *et al.* *British Journal of Anaesthesia* 1987; **59**: 1523.

Cardiovascular effects of dynorphin (1-13) and its modulation of morphine bradycardia over time. GLATT CE, KENNER JR *et al.* *Peptides* 1987; **8**: 1089.

The influence of drug polarity on the absorption of opioid drugs into CSF and subsequent cephalad migration following lumbar epidural administration. GOURLAY GK, CHERRY DA *et al.* *Pain* 1987; **31**: 297.

Effect of naloxone infusion on analgesia and respiratory depression after epidural fentanyl. GUERNERON JP, ECOFFEY C *et al.* *Anesthesia and Analgesia* 1988; **67**: 35.

Endogenous opiates: 1986. OLSON GA, OLSON RD, KASTIN AJ. *Peptides* 1987; **8**: 1135.

Spinal infusion of opiate and alpha-2 agonists in rats—tolerance and cross-tolerance studies. STEVENS CW, MONASKY MS, YAKSH TL. *Journal of Pharmacology and Experimental Therapeutics* 1988; **244**: 63.

Obstetric anaesthesia and analgesia

Mini-dose intrathecal morphine for the relief of post-caesarean section pain: safety, efficacy, and ventilatory responses to carbon dioxide. ABOUD TK, DROR A *et al.* *Anesthesia and Analgesia* 1988; **67**: 137.

Pre-eclampsia—a review of the role of prostaglandins. FRIEDMAN SA. *Obstetrics and Gynecology* 1988; **71**: 122.

Beta-adrenergic blockers in pregnancy. FRISHMAN WH, CHESNER M. *American Heart Journal* 1988; **115**: 147.

Risk factors for the occurrence of pregnancy-induced hypertension. GUZICK DS, KLEIN VR. *Clinical and Experimental Hypertension, Part B-Hypertension in Pregnancy* 1987; **6**: 281.

- Haemodynamic effects of induction of epidural analgesia in labour. HAMMOND RR, WEBSTER AC. *Canadian Journal of Anaesthesia* 1988; **35**: 41.
- Whole blood viscosity during normal pregnancy. HUISMAN A, AARNOUDSE JG *et al.* *British Journal of Obstetrics and Gynaecology* 1987; **94**: 1143.
- Red cell aggregation during normal pregnancy. HUISMAN A, AARNOUDSE JG *et al.* *British Journal of Haematology* 1988; **68**: 121.
- Uterine artery blood velocities during contractions in pregnancy and labour related to intrauterine pressure. JANBU T, NESHEIM BI. *British Journal of Obstetrics and Gynaecology* 1987; **94**: 1150.
- Acupuncture before delivery: effect on labor. LYRENAS S, LUTSCH H *et al.* *Gynecologic and Obstetric Investigation* 1987; **24**: 217.
- Hypertension in pregnancy—fetal and infant outcome. A cohort study. MONTAN S, SJOBERG NO, SVENNINGESEN N. *Clinical and Experimental Hypertension, Part B-Hypertension in Pregnancy* 1987; **6**: 337.
- Neuromuscular transmission studies in pre-eclamptic women receiving magnesium sulfate. RAMANATHAN J, SIBAI BM *et al.* *American Journal of Obstetrics and Gynecology* 1988; **158**: 40.
- Pregnancy delays paracetamol absorption and gastric emptying in patients undergoing surgery. SIMPSON KH, STAKES AF, MILLER M. *British Journal of Anaesthesia* 1988; **60**: 24.
- Whole blood platelet aggregation in normal pregnancy and pre-eclampsia. SPLAWINSKA B, SKRET A *et al.* *Clinical and Experimental Hypertension, Part B-Hypertension in Pregnancy* 1987; **6**: 311.
- Asthma and pregnancy: a prospective study of 198 pregnancies. STENIUS-AARNIALA B, PURILA P, TERAMO K. *Thorax* 1988; **43**: 12.
- Acute renal failure in pre-eclampsia-eclampsia. STRATTA P, CANAVESE C *et al.* *Gynecologic and Obstetric Investigation* 1987; **24**: 225.
- Cerebrospinal fluid levels of magnesium in patients with pre-eclampsia after treatment with intravenous magnesium sulfate: a preliminary report. THURNAU GR, KEMP DB, JARVIS A. *American Journal of Obstetrics and Gynecology* 1987; **157**: 1435.
- Myocardial infarction in pregnancy. TROUTON TG, SIDHU H, ADGEY AAJ. *International Journal of Cardiology* 1988; **18**: 35.
- Some observations of levels of plasma cholinesterase activity within an obstetric population. WHITTAKER M, CRAWFORD JS, LEWIS M. *Anaesthesia* 1988; **43**: 42.
- Plasma concentrations of bupivacaine during extradural anaesthesia for Caesarean section. The effect of adrenaline. WILSON CM, MOORE J *et al.* *Anaesthesia* 1988; **43**: 12.
- Problems and management of the pregnant women with epilepsy. YERBY MS. *Epilepsia* 1987; **28** (Suppl. 3): S29.
- Dilated cardiomyopathy in infants and children. GRIFFIN ML, HERNANDEZ A *et al.* *Journal of the American College of Cardiology* 1988; **11**: 139.
- Effect of supine posture on peak expiratory flow rates in asthma. HAFEEJE IE. *Archives of Disease in Childhood* 1988; **63**: 127.
- Facial reconstruction in Down's syndrome. HATCH DJ. *Journal of the Royal Society of Medicine* 1988; **81**: 1.
- Flow requirements and rebreathing during mechanically controlled ventilation in a T-piece (Mapleson-E) system. HATCH DJ, YATES AP, LINDAHL SGE. *British Journal of Anaesthesia* 1987; **59**: 1533.
- Neonatal neurobehavior after epidural anesthesia for cesarean section: A comparison of bupivacaine and chloroprocaine. KUHNET BR, KENNARD MJ, LINN PL. *Anesthesia and Analgesia* 1988; **67**: 64.
- Survival after cardiopulmonary resuscitation in babies of very low birth weight: is CPR futile therapy? LANTOS JD, MILES SH *et al.* *New England Journal of Medicine* 1988; **318**: 91.
- Central origin of the hypoxic depression of breathing in the newborn. MARTIN-BODY RL, JOHNSTON BM. *General Physiology and Biophysics* 1987; **6**: 25.
- Neonatal myasthenia gravis—a new clinical and immunologic appraisal on 30 cases. MOREL E, EYMARD B *et al.* *Neurology* 1988; **38**: 138.
- Respiratory and neuroendocrine responses of piglets to hypoxia during postnatal development. MOSS IR, RUNOLD M *et al.* *Acta Physiologica Scandinavica* 1987; **131**: 533.
- Prolonged apnea associated with upper airway protective reflexes in apnea of prematurity. PICKENS DL, SCHEFFT G, THACH BT. *American Review of Respiratory Disease* 1988; **137**: 113.
- Diaphragmatic and genioglossus electromyographic activity at the onset and at the end of obstructive apnea in children with obstructive sleep apnea syndrome. PRAUD JP, D'ALLEST AM *et al.* *Pediatric Research* 1988; **23**: 1.
- Atrial natriuretic peptide in infants and children. RASCHER W, BALD M *et al.* *Hormone Research* 1987; **28**: 58.
- Laryngospasm in paediatric anaesthesia. ROY WL, LERMAN J. *Canadian Journal of Anaesthesia* 1988; **35**: 93.
- Role of apnea in the sudden infant death syndrome—a personal view. SOUTHAL DP. *Pediatrics* 1988; **81**: 73.
- Plasma atrial natriuretic peptide levels in children with cardiac disease: correlation with cGMP levels and haemodynamic parameters. WEIL J, STROM TM *et al.* *Hormone Research* 1987; **28**: 64.
- Pulse oximetry versus transcutaneous pO₂ in sick newborn infants. WIMBERLEY PD, HELLEDIE NR *et al.* *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47** (Suppl. 188): 19.
- Endoscopy of the airway in infants and children. WOOD RE, POSTMA D. *Journal of Pediatrics* 1988; **112**: 1.

Paediatric anaesthesia and intensive care

- Anaesthetic considerations in facial reconstruction for Down's syndrome. BEILIN B, KADARI A *et al.* *Journal of the Royal Society of Medicine* 1988; **81**: 23.
- Effect of chronic morphine on plasma and brain beta endorphin and methionine enkephalin in pregnant rats and in their fetuses or newborn. BIANCHI M, MARINI A *et al.* *Neuroendocrinology* 1988; **47**: 89.
- The use of intravenous pancuronium bromide to produce fetal paralysis during intravascular transfusion. COPEL JA, GRANNUM PA *et al.* *American Journal of Obstetrics and Gynecology* 1988; **158**: 170.
- Cerebral monitoring in newborn infants by magnetic resonance and near infrared spectroscopy. DELPY DT, COPE MC *et al.* *Scandinavian Journal of Clinical and Laboratory Investigation* 1987; **47** (Suppl. 188): 9.
- Prenatal lidocaine and the auditory evoked responses in term infants. DIAZ M, BRANCH L *et al.* *American Journal of Diseases of Children* 1988; **142**: 160.
- Arginine vasotocin and a novel oxytocin-vasotocin-like material in plasma of human newborns. ERVIN MG, AMICO JA *et al.* *Biology of Neonate* 1988; **53**: 17.
- Cord blood acid-base status in neonates delivered by silastic vacuum cup extraction—comparison with forceps and spontaneous deliveries. GRAY DL, NELSON DM. *Obstetrics and Gynecology* 1988; **71**: 76.
- Observation of spontaneous respiratory interaction with artificial ventilation. GREENOUGH A, GREENALL F. *Archives of Disease in Childhood* 1988; **63**: 168.

Cardiovascular system

Physiology

- Factors that determine the occurrence of reperfusion arrhythmias. BOLI R, PATEL B. *American Heart Journal* 1988; **115**: 20.
- Postsynaptic alpha 1- and alpha 2-adrenergic mechanisms in coronary vasoconstriction. CHEN DG, DAI XZ *et al.* *Journal of Cardiovascular Pharmacology* 1988; **11**: 61.
- The pattern of atrial natriuretic peptide release during ventricular tachycardia in man. CROZIER IG, IKRAM H, NICHOLLS MG. *Clinical and Experimental Pharmacology and Physiology* 1987; **14**: 597.
- Systolic time intervals in diabetes mellitus. DAS AK, CHANDRASEKAR S, BALACHANDAR J. *Acta Diabetologica Latina* 1987; **24**: 283.
- Role of atrial peptide system in renal and endocrine adaptation to hypotensive hemorrhage. EDWARDS BS, ZIMMERMAN RS *et al.* *American Journal of Physiology* 1988; **254** (Part 2): R56.
- Relationship between noradrenaline reactivity and alpha-adrenoceptor density in man. FRITSCHKA E, PHILIPP T. In: ROSENTHAL J, ed. *Hormonal and neurogenic mechanisms of BP regulation*. Munich: W. Zuckschwerdt, 1987: 10.
- Multiple system organ failure. FRY DE. *Surgical Clinics of North America* 1988; **68**: 107.
- Physiology and pathophysiology of atrial peptides. GOETZ KL. *American Journal of Physiology* 1988; **245** (Part 1): E1.
- Central and peripheral catecholaminergic neurons—impact on cardiovascular regulation and mechanisms of antihypertensive drugs. GROBECKER H. In: ROSENTHAL J, ed. *Hormonal and neuro-*

- genic mechanisms of BP regulation. Munich: W. Zuckschwerdt, 1987: 1.
- Delayed myocardial ischemia following the cessation of sympathetic stimulation. HAGESTAD EL, VERRIER RL. *American Heart Journal* 1988; **115**: 45.
- Effect of cardiopulmonary bypass on circulating concentrations of leucocyte elastase and free radical activity. HIND CRK, GRIFFIN JF *et al. Cardiovascular Research* 1988; **22**: 37.
- Membrane currents in cardiac pacemaker tissue. IRISAWA H. *Experientia* 1987; **43**: 1131.
- Attenuation of the hemodynamic responses to chest physical therapy. KLEIN P, KEMPER M *et al. Chest* 1988; **93**: 38.
- Catecholamines and cardiovascular function in aging. LAKATTA EG. *Endocrinology and Metabolism Clinics of North America* 1987; **16**: 877.
- Cardiovascular effects of smoking in patients with ischemic heart disease. MYERS MG, BENOWITZ NL *et al. Chest* 1988; **93**: 14.
- Central venous pressure in humans during short periods of weightlessness. NORSK P, FOLDAGER N *et al. Journal of Applied Physiology* 1987; **63**: 2433.
- Electrocardiographic findings in myotonic dystrophy. OLOFSSON BO, FORSBERG H *et al. British Heart Journal* 1988; **59**: 47.
- Calcium channel modulation by beta-adrenergic neurotransmitters in the heart. REUTER H. *Experientia* 1987; **43**: 1173.
- Hypoxemia and hypercapnia in conscious dogs: opioid modulation of catecholamines. ROSE CE JR, LATHAM LB *et al. American Journal of Physiology* 1988; **254** (Part 2): H72.
- Role of red blood cells in the coronary microcirculation during cold blood cardioplegia. SAKAI A, MIYA J *et al. Cardiovascular Research* 1988; **22**: 62.
- Right ventricular cardiomyopathy and sudden death in young people. THIENE G, NAVA A *et al. New England Journal of Medicine* 1988; **318**: 129.
- Changes in blood pressure and plasma norepinephrine during sleep in essential hypertension. UMEMURA S, TOCHIKUBO O *et al. Japanese Circulation Journal* 1987; **51**: 1250.
- Prolonged administration of human ANP in healthy men; even-est effect on diuresis in spite of simultaneous infusion of norepinephrine. VIERHAPPER H, NOWOTNY P. *European Journal of Clinical Investigation* 1987; **17**: 544.
- Treatment and medication**
- Tocainide for drug-resistant sustained ventricular tachyarrhythmias. ADHAR GC, SWERDLOW CD *et al. Journal of the American College of Cardiology* 1988; **11**: 124.
- Naloxone requires circulating catecholamines to attenuate the cardiovascular suppression. ALLGOOD SC, GURLL NJ, REYNOLDS DV. *Journal of Surgical Research* 1988; **44**: 73.
- Antihypertensive mechanism of ketanserin in postoperative hypertension after cardiopulmonary bypass. ANGER C, CARTER JA, PRYS-ROBERTS C. *Anesthesia and Analgesia* 1988; **67**: 99.
- Improved hemodynamic function during hypoxia with bicarb, a new agent for the management of acidosis. BERSIN RM, ARIEFF AI. *Circulation* 1988; **77**: 227.
- The automatic implantable cardioverter-defibrillator—clinical experience, complications, and follow-up in 25 patients. BORBOLA J, DENES P *et al. Archives of Internal Medicine* 1988; **148**: 70.
- Inadequate subendocardial oxygen delivery during perfluorocarbon perfusion in a canine model of ischemia. CHRISTENSEN CW, REEVES WC *et al. American Heart Journal* 1988; **115**: 30.
- Role of nitrates in congestive heart failure. COHN JN. *American Journal of Cardiology* 1987; **69**: 39H.
- Blood pressure during a combination of ketanserin and hydrochlorothiazide. FERRARA LA, FASANO ML *et al. International Journal of Clinical Pharmacology Research* 1987; **7**: 463.
- Role of nitrates in acute myocardial infarction. FLAHERTY JT. *American Journal of Cardiology* 1987; **60**: 35H.
- Bevantolol: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in hypertension and angina pectoris. FRISHMAN WH, GOLDBERG RJ, BENFIELD P. *Drugs* 1988; **35**: 1.
- Pharmacokinetics and pharmacodynamics of organic nitrates. FUNG HL. *American Journal of Cardiology* 1987; **60**: 4H.
- Comparative effects of verapamil, tiapamil, diltiazem and nifedipine on systemic and splanchnic hemodynamics in man. GASIC S, EICHLER HG, KORN A. *International Journal of Clinical Pharmacology Therapy and Toxicology* 1987; **25**: 498.
- Renal effects of nadolol in cirrhosis. GATTA A, SACERDOTI D *et al. European Journal of Clinical Pharmacology* 1987; **33**: 473.
- Thrombolytic therapy of acute pulmonary embolism: current status and future potential. GOLDHABER SZ, MEYEROVITZ MF *et al. Journal of the American College of Cardiology* 1987; **10** (Suppl. B): 96B.
- Effect of heparin and contrast medium on platelet function during routine cardiac catheterisation. GREENBAUM RA, BARRADAS MA *et al. Cardiovascular Research* 1987; **21**: 878.
- Coenzyme Q10: a new drug for myocardial ischemia? GREENBERG SM, FRISHMAN WH. *Medical Clinics of North America* 1988; **72**: 243.
- Incidence of unwarranted implantation of permanent cardiac pacemakers in large medical population. GREENSPAN AM, KAY HR *et al. New England Journal of Medicine* 1988; **318**: 158.
- Amiodarone therapy: role of early and late electrophysiologic studies. GREENSPON AJ, VOLOSIN KJ *et al. Journal of the American College of Cardiology* 1988; **11**: 117.
- When 'sudden cardiac death' is not so sudden; lessons learned from the automatic implantable defibrillator. GUARNIERI T, LEVINE JH *et al. American Heart Journal* 1988; **115**: 205.
- Expired carbon dioxide—a noninvasive monitor of cardiopulmonary resuscitation. GUDIPATI CV, WEIL MH *et al. Circulation* 1988; **77**: 234.
- A randomized trial of intravenous tissue plasminogen activator for acute MI with subsequent randomization to elective coronary angioplasty. GUERCI AD *et al. New England Journal of Medicine* 1987; **317**: 1613.
- Propafenone: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in the treatment of arrhythmias. HARRON DWG, BROGDEN RN. *Drugs* 1987; **34**: 617.
- Quinidine attenuates sympathetically induced post-stenotic myocardial ischemia. SCHIPKE J, SCHULZ R *et al. Journal of Cardiovascular Pharmacology* 1987; **10**: 622.
- The effects of intraoperative blood salvage and induced hypotension on transfusion requirements during spinal surgical procedure. LENNON RL, HOSKING MP *et al. Mayo Clinic Proceedings* 1987; **62**: 1090.
- Clinical use of low molecular weight heparins and heparinoids. LEVINE MN, HIRSH J. *Seminars in Thrombosis and Hemostasis* 1988; **14**: 116.
- Can drugs reduce surgical blood loss? LEADING ARTICLE. *Lancet* 1988; **1**: 155.
- Antibiotic prophylaxis of experimental endocarditis after dental extractions. MALINVERNI R, OVERHOLSER CD *et al. Circulation* 1988; **77**: 182.
- Epidural spinal electrical stimulation in severe angina pectoris. MANNHEIMER C, AUGUSTINSSON LE *et al. British Heart Journal* 1988; **59**: 56.
- Clinical pharmacokinetics of factor VIII in patients with classical haemophilia. MESSORI A, LONGO G *et al. Clinical Pharmacokinetics* 1987; **13**: 365.
- Hemodynamic profile of BM 14 478: a new positive inotropic and vasodilating agent. MULLER-BECKMANN B, SPONER G *et al. Journal of Cardiovascular Pharmacology* 1988; **11**: 1.
- Plasma catecholamine levels in acute myocardial infarction: influence of beta-adrenergic blockade and relation to central hemodynamics. MURRAY DP, WATSON RDS *et al. American Heart Journal* 1988; **115**: 38.
- Evidence for involvement of hypocapnia and hypoperfusion in aetiology of neurological deficit after cardiopulmonary bypass. NEVIN M, COLCHESTER ACF *et al. Lancet* 1987; **2**: 1493.
- Beta-adrenergic receptors in ischemic and nonischemic myocardium: relation to ventricular fibrillation and effects of propranolol and hexamethonium. OHYANAGI M, MATSUMORI Y, IWASAKI T. *Journal of Cardiovascular Pharmacology* 1988; **11**: 107.
- High potassium levels in stored irradiated blood. RAMIREZ AM, WOODFIELD DG *et al. Transfusion* 1987; **27**: 444.
- Thrombolysis in myocardial infarction (TIMI) trial-phase 1: hemorrhagic manifestations and changes in plasma fibrinogen and the fibrinolytic system. RAO AK, PRATT C *et al. Journal of the American College of Cardiology* 1988; **11**: 1.
- Features of cardiac arrest episodes with and without acute myocardial infarction in the coronary artery surgery study (CASS). ROSS DL, DAVIS KB *et al. American Journal of Cardiology* 1987; **60**: 1219.

- Treatment of patients with symptomless left ventricular dysfunction after myocardial infarction. SHARPE N, MURPHY J *et al. Lancet* 1988; 1: 255.
- Digitalis: mechanisms of action and clinical use. SMITH TW. *New England Journal of Medicine* 1988; 318: 358.
- A simple aid to digoxin prescribing. TAGGART AJ, McDEVITT DG, JOHNSTON GD. *European Journal of Clinical Pharmacology* 1987; 33: 441.
- Effects of aprotinin on hemostatic mechanisms during cardiopulmonary bypass. VAN OEVEREN W, JANSEN NJ *et al. Annals of Thoracic Surgery* 1987; 44: 640.
- Calcium channel blockers. WEINER DA. *Medical Clinics of North America* 1988; 72: 83.

Respiration

Physiology

- Pulmonary extraction and pharmacokinetics of prostaglandin E₁ during continuous intravenous infusion in patients with adult respiratory distress syndrome. ANDREADIS NA, BONE RC *et al. American Review of Respiratory Disease* 1988; 137: 5.
- Estimates of ventilation from inductance plethysmography in sleeping asthmatic patients. BALLARD RD, KELLY PL, MARTIN RJ. *Chest* 1988; 93: 128.
- Neuropeptides in human airways—function and clinical implications. BARNES PJ. *American Review of Respiratory Disease* 1987; 136: S77.
- Effects of bronchomotor tone on static mechanical properties of lung and ventilation distribution. CROWFORD ABH, MAKOWSKA M, ENGEL LA. *Journal of Applied Physiology* 1987; 63: 2278.
- Causes of error of respiratory pressure-volume curves in paralyzed subjects. DALL'AVA-SANTUCCI J, ARMAGANIDIS A *et al. Journal of Applied Physiology* 1988; 64: 42.
- Distributions of vascular volume and compliance in the lung. DAWSON CA, RICKABY DA *et al. Journal of Applied Physiology* 1988; 64: 266.
- The biosynthesis of regulatory peptides. DOCKRAY GJ. *American Review of Respiratory Disease* 1987; 136: S9.
- Flow limitation and wheezes in a constant flow and volume lung preparation. GAVRIELY N, GROTEBERG JB. *Journal of Applied Physiology* 1988; 64: 17.
- Pulmonary extraction of PGE₁ in the adult respiratory distress syndrome. GILLIS CN. *American Review of Respiratory Disease* 1988; 137: 1.
- Aerosol anesthesia increases hypercapnic ventilation and breathlessness in laryngectomized humans. HAMILTON RD, WINNING AJ *et al. Journal of Applied Physiology* 1987; 63: 2286.
- Effects of metabolic blockade on distribution of blood flow to respiratory muscles. JOHNSON RL JR, REID MB. *Journal of Applied Physiology* 1988; 64: 174.
- Adult respiratory distress syndrome as a specific manifestation of a general permeability defect in trauma patients. KREUZFELDER E, JOKA T *et al. American Review of Respiratory Disease* 1988; 137: 95.
- Effect of the diaphragmatic contraction on lower oesophageal sphincter pressure in man. MITTAL RK, ROCHESTER DF, MCCALLUM RW. *Gut* 1987; 28: 1564.
- Pulmonary vasomotor responses to neural activation in man. MORUZZI P, SGANZERLA P, GUZZI MD. *Cardiovascular Research* 1988; 22: 25.
- Effect of body posture on respiratory impedance. NAVAJAS D, FARRE R *et al. Journal of Applied Physiology* 1988; 64: 194.
- Breathing pattern of anesthetized humans during pancuronium-induced partial paralysis. NISHINO T, YOKOKAWA N *et al. Journal of Applied Physiology* 1988; 64: 78.
- Experimental diabetes and the lung. I. Changes in growth, morphometry, and biochemistry. OFULUE AF, KIDA K, THURLBECK WM. *American Review of Respiratory Disease* 1988; 137: 162.
- Peptide receptors in the airways. REGOLI D. *American Review of Respiratory Disease* 1987; 136: S35.
- Effects of high-frequency jet ventilation on arterial baroreflex regulation of heart rate. ROUBY JJ, HOUISSA M *et al. Journal of Applied Physiology* 1987; 63: 2216.
- Factors contributing to bronchial hyper-responsiveness in asthma. SNASHALL PD, GILLET MK, CHUNG KF. *Clinical Science* 1988; 74: 113.
- Influence of pulmonary inflations on discharge of pontile respira-

- tory neurons. ST JOHN WM. *Journal of Applied Physiology* 1987; 63: 2231.
- Neuropeptides and immunity. STANISZ A, SCICCHITANO R *et al. American Review of Respiratory Disease* 1987; 136: S48.
- Bilateral diaphragm paralysis and sleep apnoea without diurnal respiratory failure. STRADLING JR, WARLEY ARH. *Thorax* 1988; 43: 75.
- Lung mechanics and neuromuscular output during carbon dioxide inhalation after airway anesthesia. SULLIVAN TY, DEWEESE EL *et al. Journal of Applied Physiology* 1987; 63: 2542.
- Oronasal obstruction lung volumes and arterial oxygenation. SWIFT AC, CAMPBELL IT, MCKOWN TM. *Lancet* 1988; 1: 73.
- Hypoxia enhances unilateral lung injury by increasing blood flow to the injured lung. TAKEDA K, KNAPP MJ *et al. Journal of Applied Physiology* 1987; 63: 2516.
- Neuropeptides in the airways—a review. UDDMAN R, SUNDLER F. *American Review of Respiratory Disease* 1987; 136: S3.

Treatment and medication

- Does aminophylline improve nocturnal hypoxia in patients with chronic airflow obstruction? EBDEN P, VATHENEN S. *European Journal of Respiratory Disease* 1987; 71: 384.
- Efficiency of plasma exchange in Guillain-Barre Syndrome: role of replacement fluids. FRENCH CO GROUP ON PLASMA EXCHANGE. *Annals of Neurology* 1987; 22: 753.
- Bitolterol: a preliminary review of its pharmacological properties and therapeutic efficacy in reversible obstructive airway disease. FRIEDEL HA, BROGDEN RN. *Drugs* 1988; 35: 22.
- Moderate hypoxia: reactivity of pial arteries and local effect of theophylline. HALLER C, KUSCHINSKY W. *Journal of Applied Physiology* 1987; 63: 2208.
- A new method for separate lung ventilation. NAZARI S, TRAZZI R *et al. Journal of Thoracic and Cardiovascular Surgery* 1988; 95: 133.
- The acute haemodynamic effects of intravenous verapamil in patients with chronic obstructive airways disease. TREACHER DF, DOUGLAS A *et al. Quarterly Journal of Medicine* 1987; 65: 941.
- Can pulmonary vasodilators improve survival in cor pulmonale due to hypoxic chronic bronchitis and emphysema? WHYTE KF, FLENLEY DC. *Thorax* 1988; 43: 1.

Central nervous system

Physiology

- Effects of hypotension induced with sodium nitroprusside on the cerebral circulation before, and one week after, the subarachnoid injection of blood. FITCH W, PICKARD JD *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1988; 51: 88.
- Effect of hemorrhagic shock upon spinal cord blood flow and evoked potentials. HITCHON PW, LOBOSKY JM *et al. Neurosurgery* 1987; 21: 849.
- Corticospinal direct response in humans—identification of the motor cortex during intracranial surgery under general anaesthesia. KATAYAMA Y, Tsubokawa T *et al. Journal of Neurology, Neurosurgery and Psychiatry* 1988; 51: 50.
- Increases in cerebral cortical perfusate adenosine and inosine concentrations during hypoxia and ischemia. PHILLIS JW, WALTER GA *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; 7: 679.
- Effect of adenosine on human cerebral blood flow as determined by positron emission tomography. SOLLEVI A, ERICSON K *et al. Journal of Cerebral Blood Flow and Metabolism* 1987; 7: 673.
- Evolution of neurotransmitter receptor systems. VENTER JC, DI PORZIO U *et al. Progress in Neurobiology* 1988; 30: 105.
- Abnormal diurnal variation in salt and water excretion in patients with obstructive sleep apnoea. WARLEY ARH, STRADLING JR. *Clinical Sciences* 1988; 74: 183.

Treatment and medication

- Recent Advances in Pharmacotherapy—migraine. EDMEDS JG. *Canadian Medical Association Journal* 1988; 138: 107.
- Pharmacology of antiepileptic drugs. FERRENDELLI JA. *Epilepsia* 1987; 28 (Suppl. 3): S14.
- A controlled trial of nimodipine in acute ischemic stroke. GELMERS

- HJ, GORTER K *et al.* *New England Journal of Medicine* 1988; **318**: 203.
- Predictive value of Glasgow coma score for awakening after out-of-hospital cardiac arrest. MULLIE A, VERSTRINGE P *et al.* *Lancet* 1988; **1**: 137.
- Continuous duodenal infusions of levodopa: plasma concentrations and motor fluctuations in Parkinson's disease. SAGE JJ, SCHUH L *et al.* *Clinical Neuropharmacology* 1988; **11**: 36.
- Anticonvulsant drugs and cognitive function: a review of the literature. TRIMBLE MR. *Epilepsia* 1987; **28** (Suppl. 3): S37.

Endocrine and metabolic

Physiology

- Bioactivation mechanisms and hepatocellular damage. ANDERS MW. In: ARIAS IM, POPPER H, eds. *Liver biology and pathology*, 2nd edn. New York: Raven Press, 1988: 389.
- Effect of elective surgical procedures on tissue protein synthesis. BAKIC V, MACFADYEN BV, BOOTH FW. *Journal of Surgical Research* 1988; **44**: 62.
- Gastrointestinal metabolic effects of amylase inhibition in diabetics. BOIVIN M, FLOURIE B *et al.* *Gastroenterology* 1988; **94**: 387.
- A model of the distribution and metabolism of corticotropin-releasing factor. CANDAS B, LALONDE J, NORMAND M. *American Journal of Physiology* 1988; **254** (Part 1): E104.
- Physiologic and pharmacologic studies of atrial natriuretic factor—a natriuretic and vasoactive peptide. CODY RJ, ATLAS SA, LARAGH JH. *Journal of Clinical Pharmacology* 1987; **27**: 927.
- Circulating opioid peptides during water immersion in normal man. CORUZZI P, RAVANETTI CC *et al.* *Clinical Sciences* 1988; **74**: 133.
- Cardiovascular actions of vasopressin. COWLEY AW, LIARD JF. In: GASH DM, BOER GJ, eds. *Vasopressin—principles and properties*. New York: Plenum Publishing, 1987: 389.
- The kidney in liver disease. EPSTEIN M. In: ARIAS IM, POPPER H, eds. *Liver: biology and pathobiology*, 2nd edn. New York: Raven Press, 1988: 1043.
- Ability of corticotropin releasing hormone to stimulate cortisol secretion independent from pituitary adrenocorticotropin. FEHM HL, HOLL R *et al.* *Life Sciences* 1988; **42**: 679.
- Growth hormone responses to pyridostigmine in normal adults and in normal and short children. GHIGON E, MAZZA E *et al.* *Clinical Endocrinology* 1987; **27**: 669.
- Microproteinuria: response to operation. GOSLING P, SHEARMAN C *et al.* *British Medical Journal* 1988; **296**: 338.
- Renal function in fulminant hepatic failure—haemodynamics and renal prostaglandins. GUARNER F, HUGHES RD *et al.* *Gut* 1987; **28**: 1643.
- Control of water balance in infants with bronchopulmonary dysplasia: role of endogenous vasopressin. HAZINSKI TA, BLALOCK WA, ENGELHARDT B. *Pediatric Research* 1988; **23**: 86.
- Detoxication—conjugation and hydrolysis in the liver. JAKOBY WB. In: ARIAS IM, POPPER H, eds. *Liver: biology and pathobiology*, 2nd edn. New York: Raven Press, 1988: 375.
- The effects of metabolic acidosis on renal function of fetal sheep. KESBY GJ, LUMBERS ER. *Journal of Physiology* 1988; **396**: 65.
- A standard nomenclature for the structures of the kidney. KRIZ W. *American Journal of Physiology* 1988; **254** (Part 2): F1.
- Predisposition to hypertension and susceptibility to renal disease in insulin-dependent diabetes mellitus. KROLEWSKI AS, CANESSA M *et al.* *New England Journal of Medicine* 1988; **318**: 140.
- Pressor inhibition of angiotensin-induced ACTH secretion. KUCHARCZYK J, COWAN J, LAYBERRY R. *Canadian Journal of Physiology and Pharmacology* 1987; **65**: 2308.
- Crohn's disease with respiratory tract involvement. LEMANN M, MESSING B *et al.* *Gut* 1987; **28**: 1669.
- Vasopressin, oxytocin, dynorphin, enkephalin and corticotrophin-releasing factor mRNA stimulation in the rat. LIGHTMAN SL, YOUNG WS III. *Journal of Physiology* 1987; **394**: 23.
- Selective agonists and antagonists of vasopressin. MANNING M, BANKOWSKI K, SAWYER WH. In: GASH DM, BOER GJ, eds. *Vasopressin—principles and properties*. New York: Plenum Publishing, 1987: 335.
- Pressor and intestinal vascular bed responses to vasopressin after cholinergic blockade. MARTIN DS, MCNEIL JR. *American Journal of Physiology* 1988; **254** (Part 2): H45.
- Steroid hormone receptors—recent advances. MOUDGIL VK. In: MOUDGIL VK ed. *Recent advances in steroid hormone action*. Berlin: Walter de Gruyter, 1987: 1.
- Hepatic detoxification and hepatic function in chronic active hepatitis with and without cirrhosis. MUTING D, KALK JF *et al.* *Digestive Diseases and Sciences* 1988; **33**: 41.
- Effects of water immersion on arginine vasopressin release in humans. NORSK P, EPSTEIN M. *Journal of Applied Physiology* 1988; **64**: 1.
- Biosynthesis of vasopressin and neurophysins. NORTH WG. In: GASH DM, BOER GJ, eds. *Vasopressin—principles and properties*. New York: Plenum Publishing, 1987: 175.
- Plasma AVP and renal concentrating defect in chloride depletion metabolic alkalosis. PETERSON LN, SZTORE D *et al.* *American Journal of Physiology* 1988; **254** (Part 2): F15.
- Control of blood-gas and acid-base status during isometric exercise in humans. POOLE DC, WARD SA, WHIPP BJ. *Journal of Physiology* 1988; **396**: 365.
- GH feedback occurs through modulation of hypothalamic somatostatin under cholinergic control: studies with pyridostigmine and GHRH. ROSS RJM, TSAGARAKIS S. *Clinical Endocrinology* 1987; **27**: 727.
- Vasopressin: a model for the study of effects of additives on the oral and rectal administration of peptide drugs. SAFFRAN M, BEDRA C *et al.* *Journal of Pharmaceutical Sciences* 1988; **77**: 33.
- ATP synthesis by oxidative phosphorylation. SENIOR AE. *Physiological Reviews* 1988; **68**: 177.
- Effects of neurotransmitters and neuropeptides on vasopressin release. SLADEK CD, ARMSTRONG WE. In: GASH DM, BOER GJ, eds. *Vasopressin—principles and properties*. New York: Plenum Publishing, 1987: 275.
- The reduction of renin and aldosterone as a response to acute hypovolemia is blocked by a monoclonal antibody directed against ANP. STASCH J-P, HIRTH C *et al.* *Life Sciences* 1988; **42**: 511.
- Physiological effects of vasopressin on the kidney. VALTIN H. In: GASH DM, BOER GJ, eds. *Vasopressin—principles and properties*. New York: Plenum Publishing, 1987: 369.
- Antibodies to vasopressin in patients with diabetes insipidus: implications for diagnosis and therapy. VOKES TJ, GASKILL MB, ROBERTSON GL. *Annals of Internal Medicine* 1988; **108**: 190.
- Interactions between the neuroendocrine and immune systems: common hormones and receptors. WEIGENT DA, BLALOCK JE. *Immunological Reviews* 1987; **100**: 79.
- Effect of adrenal function on gastrointestinal peptide release in experimental cardiac arrest. WORTSMAN J, FOLEY PJ *et al.* *Journal of Laboratory and Clinical Medicine* 1988; **111**: 104.
- Detoxication—oxidation and reduction in the liver. ZIEGLER DM. In: ARIAS IM, POPPER H, eds. *Liver: biology and pathobiology*, 2nd edn. New York: Raven Press, 1988: 363.

Treatment and medication

- Lack of hypoglycemic symptoms and decreased beta-adrenergic sensitivity in insulin-dependent diabetic patients. BERLIN I, GRIMALDI A *et al.* *Journal of Clinical Endocrinology and Metabolism* 1988; **66**: 273.
- l-Desamino-8-D-arginine vasopressin (desmopressin) shortens the bleeding time in storage pool deficiency. NIEUWENHUIS HK, SIXMA JJ. *Annals of Internal Medicine* 1988; **108**: 65.
- Clinical pharmacokinetics and endocrine disorders: therapeutic implications. O'CONNOR P, FEELY J. *Clinical Pharmacokinetics* 1987; **13**: 345.
- The use of calcium antagonists in patients with renal failure. RAHN KH, VAN BORTEL LM, MOOY JM. *Journal of Hypertension* 1987; **5** (Suppl. 4): S67.
- Hypertension, blood viscosity, and cardiovascular morbidity in renal failure: implications of erythropoietin therapy. RAINE AEG. *Lancet* 1988; **1**: 97.
- Kinetics of potassium excretion following oral supplements: evidence of induced natriuresis. RAKHT A, MELETHIL S *et al.* *Pharmaceutical Research* 1987; **4**: 531.
- Effect of a new somatostatin analogue SMS 201-995 (Sandostatin) on the renin-aldosterone axis. SIEBER C, GNADINGER M *et al.* *Clinical Endocrinology* 1988; **28**: 25.
- Pharmacokinetics of amiloridine in renal and hepatic disease.

SPAHN H, REUTER K *et al.* *European Journal of Clinical Pharmacology* 1987; **33**: 493.

Pain

Physiology

Acute and chronic pain in hemophilia. CHOINIERE M, MELZACK R. *Pain* 1987; **31**: 317.

Treatment and medication

Dexamethasone alters plasma levels of beta-endorphin and post-operative pain. HARGREAVES KM, SCHMIDT EA *et al.* *Clinical Pharmacology and Therapeutics* 1987; **42**: 601.

Low dose epidural morphine does not affect non-nociceptive spinal reflexes in patients with postoperative pain. WILLER JC, BERGERET S *et al.* *Pain* 1988; **32**: 9.

Other

Physiology

Gastric fluid volume and pH in elective inpatients. Part 1: coffee or orange juice versus overnight fast. HUTCHINSON A, MALTBY JR, REID CRG. *Canadian Journal of Anaesthesia* 1988; **35**: 12.

Index of computer programs

032.1.32

Author G.N.C. Kenny

Conversion to Locomotive Basic by R.M. Tackley.

Title CALREAD (for the Amstrad CPCs)

Description This program will allow Amstrad computer users to take advantage of the CAL text files already written and distributed via 'FABB' by the Faculty of Anaesthetists.

Language Locomotive basic

Computing facility Amstrad CPC Microcomputers with a disc drive.

030.2.31

Authors D.P. Burridge, J. Hawkrigg, A. Rennison

Title Emergency First Aid (A Save-A-Life disc)

Description A basic CPR teaching tool aimed at schoolchildren, nurse training and at promoting the training of emergency ambulancemen. Most doctors will learn something and anaesthetists argue over the correct answers to the M.C.Q. The basic resuscitation techniques are illustrated by innovative animated diagrams.

Language BBC Basic

Computing facility BBC micro (any model) with disc drive.

Availability Disc £6, Cassette (text only) £3. Touch screen and multiple user (school) versions available from the principal author; Birch Hill Hospital, Rochdale, Lancashire.

032.2.32

Author R.M. Tackley

Title IVDRUGS (Pharmacokinetics)

Description A pharmacokinetic teaching program. Drug concentrations are plotted according to an imaginary 2-compartment model, and the student is invited to see the effects of changing dose regimens and/or kinetic parameters. Appropriate explanations are given throughout.

Language Locomotive basic on BBC Basic

Computing Any Amstrad CPC with disc drive or BBC micro.

Availability This program is available via the FABB system.

Dr J.G. Davies (*Department of Anaesthesia, Royal Lancaster Infirmary, Lancaster, LA1 4RP*) has assumed responsibility for the preparation of this item. Please send details of your programs to him. They should be relevant to anaesthesia, intensive care, basic sciences or teaching.

Safety Information Bulletin

These are issued regularly by the Department of Health and Social Security

Flash fire in an anaesthetic machine (SIB) 88 (2)

An MIE anaesthetic machine was involved in a flash oxygen fire recently. The machine which was 18 years old did not conform to British or International standards. The fire was believed to be due to the failure of the non-return valve in the yoke used for pipe line supply. The machine

had been regularly serviced, and more than 5 years ago the supplier recommended that the anaesthetic machine needed to be replaced since it was uneconomical to service the equipment. Users are again warned about the dangers of old obsolete equipment which may be unreliable, worn out, or damaged beyond repair.

Erratum

Anaesthesia, 1988, Volume 43, pages 205–206

Injury to the axillary nerve

C.L. GWINNUTT

Towards the end of the Discussion, at the bottom of the first column on page 206, the description of the load-bearing anatomical points was confused. Most of the weight is borne by the knees and the ischial spines because the latter rest on the support. The more usual support offered by the anterior superior iliac spines is not operative in this modified position because the table is also tilted 20° head up.

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Manuscripts will be reviewed for possible publication on the understanding that they are being submitted to one journal at a time and have not been published, simultaneously submitted, or already accepted for publication elsewhere. This does not preclude consideration of a manuscript that has been rejected by another journal or of a complete report that follows publication of preliminary findings elsewhere, usually in the form of an abstract. Investigations performed on man must conform to appropriate ethical standards including voluntary, informed consent and acceptance by an ethical committee. Articles accepted become copyright of *Anaesthesia*.

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Dr J. N. Lunn, Editor of *Anaesthesia*, Department of Anaesthetics, University Hospital of Wales, Heath Park, Cardiff CF4 4XW, UK.

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(continued overleaf)

Examples of correct form of references
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JOURNAL

Standard journal article—(List all authors)

SOTER NA, WASSERMAN SI, AUSTEN KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *New England Journal of Medicine* 1976; **294**: 687-90.

Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36**: 119-25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5**: 224-5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. *Complement: mechanisms and functions*. New York: Prentice-Hall, 1976.

Corporate authors

American Medical Association Department of Drugs. *AMA drug evaluations*, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, comps. *Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L, SWARTZ MN. Pathogenic properties of invading micro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W.B. Saunders, 1974: 457-72.

Agency publication

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series 10*: Data from the National Health Survey, No. 69) [DHEW publication No. (HSM) 72-1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUCHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66-81.

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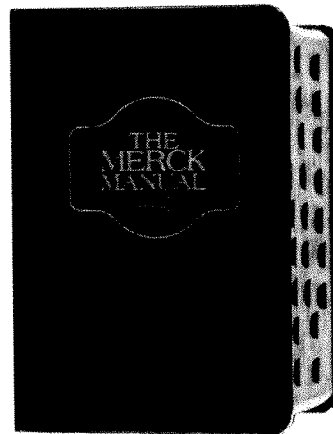
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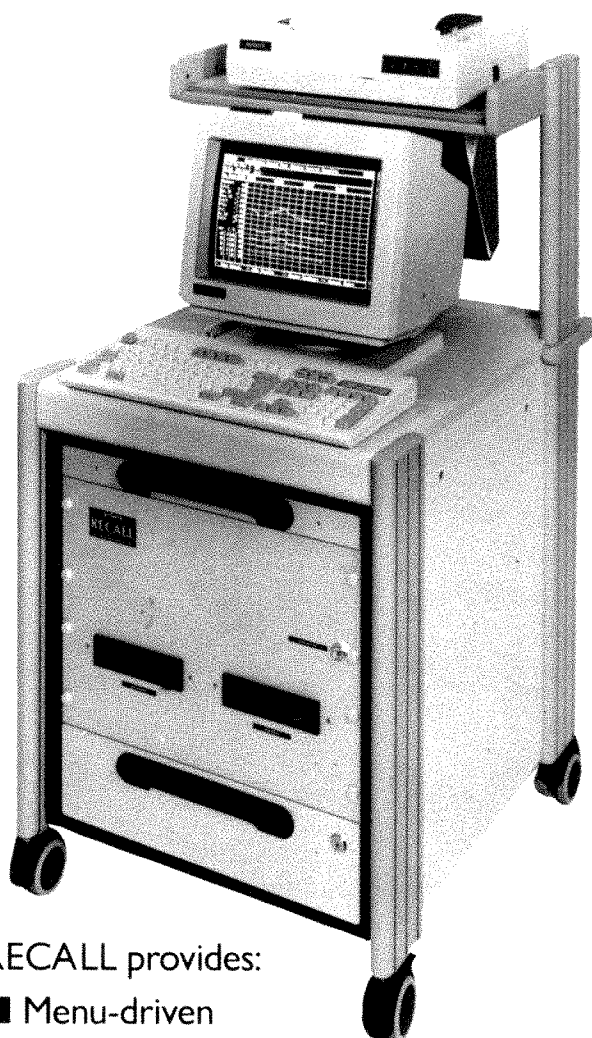
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In addition, a range of user-definable menus allows intra-operative details to be entered with a few keystrokes.

Comments and drug administrations are timed automatically.

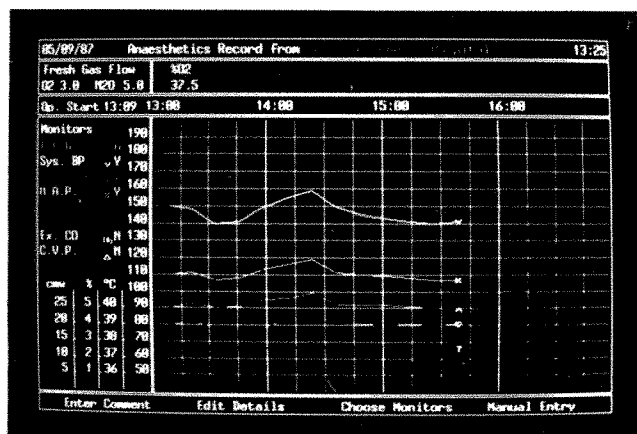
At the end of the operation RECALL prints a full anaesthetics record, and all data are stored in a secure computer database from where they can be retrieved in seconds.



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Real-time trended display of vital signs – each measure is integrated on a single screen. Comments can be typed in during the operation for later review.

Intra-operative details – all anaesthetics procedures can be recorded. Entries can be typed in when not listed in the menus.

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